FDA CTP - Third Party Governance of Industry-Sponsored Tobacco Product Research: A Public Workshop

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A Matter of Record
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FOOD AND DRUG ADMINISTRATION
CENTER FOR TOBACCO PRODUCTS

THIRD PARTY GOVERNANCE OF INDUSTRY-SPONSORED TOBACCO PRODUCTS RESEARCH: A PUBLIC WORKSHOP

Wednesday, March 20, 2013
8:30 a.m. to 12:50 p.m.

9200 Corporate Boulevard
Rockville, Maryland

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C O N T E N T S

P R O C E E D I N G S
(8:30 a.m.)

MS. DILLEY: We have a just a few people checking in still, so we'll take another couple of minutes, and then we'll get started.

Introduction

DR. ASHLEY: I think we may have a few people continuing to wander in, but we're going to go ahead and get started.

Welcome back to our second day of FDA's public workshop on Third Party Governance of Industry-Sponsored Tobacco Product Research. Yesterday, we had a series of fruitful and what I thought was very interesting discussions. We first heard from Daniel Carpenter about the IOM committee's deliberations and recommendations regarding third-party governance. It's really served to provide some useful context and to kind of frame the topics and discussion over the two-day workshop.

A couple of things I took out of that directly was really the impact of the Swedish Match

letter, which came to IOM and kind of got them started on thinking about these issues and also, really about their concern about vulnerable subpopulations and the challenges in doing any kind of studies related to vulnerable subpopulations.

We then heard from a range of interested parties in the academic research and public health communities about the challenges of conducting industry-sponsored tobacco product research. We heard a number of comments about the challenges of history, the history of research being sponsored by the tobacco industry and also differences between general research areas and product-specific research, and kind of the challenges in looking at those two different aspects as we consider that. And also, we heard some discussion about challenges of really accepting industry funding to do research in the academic communities and what that presented for them.

We also heard two examples of independent review that have been used in other arenas, followed by a discussion of the aspects of those

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approaches. Some of those may or may not apply to what we're doing here, but they were kind of different things. They brought up a number of things for us to consider.

As the IOM noted, there's really no independent entities to fulfill these roles for the tobacco industry, so there's really not a good example for us to basically say we will adopt that. But we will try to use those two examples as things we might learn some things from.

We talked about concern with the challenge of opening up data to the public and having the transparency issue around data and how the public may respond and how the public may evaluate data and the challenges and the concerns about doing that for an organization.

Today, we'll be starting the meeting with a public comment session, followed by a continuation of the discussion of the challenges in conducting industry-sponsored tobacco product research. I look forward to continued discussions on the issue.

I'm now going to turn it back over to Abby

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Dilley. She's going to give us -- because we've got some new folks in the audience, she's going to kind of give us a little bit of what we heard yesterday about kind of the ground rules of what we're working under, and I'll let Abby take it from here. Thank you.

MS. DILLEY: Thanks, David.

Good morning. My name is Abby Dilley, and I work for an organization named RESOLVE, a nonprofit organization based here in D.C. And my colleague Beth Weaver and I, along with some of the CTP staff, are here to help support what we hope will be a productive second day of this workshop, and really to help support the primary goals of this session, which are to gather as much input and information regarding the development of credible research on modified-risk tobacco products and the use of third-party governance structures for those products, as well as a broader discussion of some of the issues around research.

So I just wanted to go over a couple of things, as David mentioned, given that we do have

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some new people in terms of the organization. David's already given you the content of the discussion today and a brief review of yesterday. Most of you were here for that, and some of those online, also, but I just want to go over a few things.

So in order to gather as much information as possible, we have three different ways of doing that. We have public comment period, and David referenced we'll be doing that right after we go over a few of the preliminaries. We also have presentations today similar to yesterday. The presenters will have around 10, 15 minutes of time for their presentations, and then we'll take some brief Q&A just for questions of clarity.

Then there will also be after each of -- well, the main panel today -- not after public comment period, we don't Q&A after that. But we do have Q&A at the end of the day at the end of the panel.

So we'll take a break after I think we have two speakers initially, and then we have a series

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of five speakers. And I just want to remind people on the agenda that there's a little typo in there. I think we had a 45-minute break. We don't. We have a 15-minute break so we have a little bit more time for the series of the last section of presenters on that panel. And then, again, we'll have approximately 45 minutes to an hour for a question-and-answer period. And then we'll have some final comments, some thank yous, and we'll adjourn no later than 1:00.

So my role as moderator is to keep us on track and on time and on task. And we have the lights for the speakers to just give them a range of their time, and that seemed to work very well yesterday, and then also, to do some follow-up questions. As I mentioned yesterday, I've done some work in this area. I know some of the issues, but I'm certainly not an expert. So please correct me if I repeat a question or from the e-mail; certainly feel free to follow up.

Those of you who are submitting questions, we strongly encourage you to do that. We did take

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questions from e-mails yesterday, so we'd like to continue to do that so that, again, all for the purpose of gathering as much information and input, just so we can be sure to get as much information as possible.

Similar to yesterday, we'd like to use some just basic meeting protocols in terms of staying on topic and task around these issues. Be brief and to the point with questions. I thought people did great yesterday. Again, we're really trying to get to as many questions. I don't think we ever ran out of -- maybe there were one or two times where people had a couple of additional questions, but I think we got to as many as we could yesterday.

Again, if you do have additional comments or questions that we don't get to, there are cards over there to submit some additional questions. There's also going to be, as follow-up to this meeting, the webcast will be archived. There will be a transcript, and then there will also be a public docket that will be opened, and people can submit additional comments when that docket is open

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on this topic. So, again, trying to encourage as much input as possible.

Lastly, just being respectful of everyone's time. And certainly in keeping with yesterday, there were certainly some strong opinions around this topic and the issues associated with that, and I think we can do it in a respectful manner. That I think was certainly the case yesterday and continue that today.

Just in terms of helping, encourage everybody being able to hear the conversation, to turn your cell phones off, any electronic devices. If you haven't already done that, we'd appreciate it.

Then also, if you have conversations with people, if you could do that outside or wait for a break. It's just distracting when people are trying to hear the presentations, and just to make sure we're having one conversation in the room, it helps quite a bit to do that.

I don't think there are members of the media here, but if there are, similar structure to

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yesterday. Raquel Ortiz is in the back. If there's any interest in setting up interviews with CTP staff or FDA staff, she's the person to talk with to go through the appropriate channels to do that. For others, certainly, you can talk to others as you want to. But, again, we would ask that you do that at the break and outside the room so we can keep the discussion focused inside the room.

Hopefully, when you came through yesterday -- today -- that you picked up your materials. There were slides from yesterday, and now there are slides for today, the presenters this morning, out there. So if you haven't gotten those, there are copies out there.

There's also the agenda, and then the feedback form. So would appreciate feedback from anyone and everyone who could provide that. And the box up here again is for those forms, so please do fill those out.

Any questions about our agenda today?

(No response.)

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Public Comment Session

MS. DILLEY: So as we mentioned, we'll move right into the public comments section of the agenda. And we have three people who pre-registered per the notice today. We're going to have them come up here and use the microphone up here. They'll have 10 minutes per person, so they'll have the light system as well. It'll give you a yellow and a red as you get close to your 10 minutes, if they go to that length of time.

I think the first speaker that was signed up is Sharon Eubanks. Sharon. Okay. You're here. Good. So come on up, and we will start the public comment period. Thank you for coming.

MS. EUBANKS: Good morning. I'm here to read letters that Ruth Malone provided, Ruth Malone, UCSF, department of social and behavioral sciences, directed to Center for Tobacco Products, Food and Drug Administration, dated January 20, 2013.

"Dear Colleagues, I was very surprised to be invited to present as part of an FDA sponsored,

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quote, unquote, 'facilitated dialogue panel' also featuring tobacco industry representatives, which would be focused on the topic of industry-funded research. This very type of industry engagement with senior public health officials is straight out of the tobacco companies' public relations, quote, unquote, 'corporate social responsibility playbook,' and was something that at least one tobacco company anticipated as a favorable result of FDA legislation."

I'm going to omit the footnotes for purposes of time.

"Such dialogues have been part of this and earlier industry public relations campaigns. Public health authorities and scientists, to say nothing of the federal agency charged with regulating this industry, should not lend their legitimacy to the tobacco companies' efforts to position themselves as socially responsible.

"I would be very willing to come to Rockville and share my perspectives with the FDA on the issue of third party and tobacco products

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research. However, I cannot in good conscience participate as a panelist in this facilitated dialogue with the tobacco industry. Further, I strongly urge that other researchers from the public health community decline participation on such panels. The FDA should consider other means of determining a suitable framework for addressing the many issues related to industry-funded research.

"While this is clearly an issue about which I have thought and written extensively, I think this meeting as currently envisioned is a very bad idea. My reasons are, first, involving the tobacco companies as stakeholders on the panel with the public health community in this way suggests that all parties share a common or at least congruent role. This is a flawed assumption.

"Public health advocates, and presumably, the FDA, have a stake in saving lives. Tobacco companies have a stake in protecting profits. The research evidence has repeatedly demonstrated that they will do whatever it takes to continue to

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promote the use of cigarettes, their single most deadly product. While the companies may have an interest in reducing the numbers who die prematurely from using their products so that they will live to purchase more of them, they have never indicated any willingness to pull from the market the products that kill half their longtime users and continue to be sold. Absent such willingness, the practical goals of public health and the tobacco industry are in direct conflict. No dialogue will change that.

"Second, any such discussion among stakeholders would require minimal level of mutual understanding about the nature and purpose of science. However, a large body of academic research, based on the industry's own internal documents, as well as federal Judge Gladys Kessler's extensive findings of fact in the successful U.S. Department of Justice racketeering case against the major tobacco companies demonstrates that research is an arena in which the tobacco industry is particularly untrustworthy.

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"This fact is also repeatedly noted in the Institute of Medicine's report on scientific standards for studies on modified-risk tobacco products. As the Kessler decision found, the tobacco industry engaged in a conspiracy to cover up and distort the evidence of their product's harmfulness, and they have a long track record of egregious manipulation of science. The courts also found that this behavior is continuing and likely to continue in the future. I see no reason to differ with this conclusion.

"For this very reason, Tobacco Control, the journal that I edit, and other reputable scientific journals, including Plus Medicine, no longer publish tobacco-industry-funded research. To engage the industry as a legitimate partner in the discussion of how we deal with industry science is to ignore this large body of evidence.

"Third, as noted briefly above, such engagements have long been envisioned by tobacco companies as facilitating their image reform efforts while creating divisions within the tobacco

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control community. As we demonstrated in our papers examining Philip Morris' support for FDA regulation of tobacco products and its development of Project Sunrise, which sought to create and exploit divisions within tobacco control, engagement with public health organizations allows tobacco companies to position themselves as reasonable and responsible and position those who refuse to engage as extremists.

"In fact, shortly after the failure of a previous bill giving FDA authority to regulate tobacco, top Philip Morris executives were exploiting public speaking opportunities in which they falsely claimed to have partnered with leading public health organizations in supporting regulation. This is precisely the type of mileage tobacco companies can achieve from engaging in facilitated dialogues such as those envisioned by the FDA.

"Fourth, tobacco industry demoralization is a key part of successful tobacco control efforts. Convening a meeting of this sort undermines those

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critically important efforts by creating a forum for re-legitimization through association with respected public health agencies and leaders. Lending the FDA imprimatur to a public meeting featuring tobacco company speakers suggests that something has indeed changed and the industry is no longer harming people through its promotion of deadly products, but this is patently untrue.

"And as we recently showed in an extensive review, a robust body of evidence supports tobacco industry demoralization as an effective population-level tobacco control strategy that contributes to reduced smoking prevalence among young people, reduced youth smoking initiation, increased intentions to quit, and reduced perceived peer smoking prevalence. It is very puzzling that the FDA would act in a way that undermines this important work.

"The FDA may be required to interact with industry for the purposes of discussing proposed regulation of tobacco products and what tobacco companies must do to comply. The FDA is not,

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however, required to facilitate dialogue as though it were acting as a neutral mediator between two parties with equally valid but divergent interests.

"In positioning itself as some sort of neutral party, FDA is unwittingly acting as an agent for the tobacco industry's public relations initiatives and undermining a strong tobacco control strategy. This is very problematic, and those of us who have spent more than a decade researching industry strategies, enormously naive.

"For those reasons, I am declining to participate in this meeting and urging my colleagues to do the same. Sincerely, signed, Ruth E. Malone, RN, PhD, FAAN, professor and chair, Department of Social and Behavioral Sciences, editor, Tobacco Control."

Letter dated February 6, 2013 from Ruth Malone, University of California San Francisco, directed to Lawrence Dayton, MD, director, Center for Tobacco Products.

"Dear Dr. Dayton and tobacco control colleagues, I do appreciate the attempts of the

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Center for Tobacco Products to respond to the issues raised in my previous letter declining the invitation to be part of the planned dialogues panel with the tobacco industry. While I applaud the dropping of the facilitated dialogues meeting characterization, the proposed revised format, which clusters invited presenters from government, academics, and public health representatives on day 1, followed by invited presentations from the tobacco industry on day 2, does not adequately address the substantive issues raised by my letter. It remains the same meeting with the same agenda and purpose, merely rearranging the program.

"Therefore, I must again respectfully and regretfully decline your invitation to attend this particular meeting. The first point raised in my previous letter related to regarding tobacco companies as equivalent stakeholders with public health. I see nothing in the revised format that changes this since public health and tobacco company representatives continue to be placed on the same meeting agenda as co-equals, albeit now on

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different days.

"Tobacco companies are stakeholders only in the promotion of tobacco product use, not promoting public health, which is the purpose of the Family Smoking Prevention and Tobacco Control Act. While the tobacco companies have every right to express their opinions and submit materials for the FDA's consideration, you are not required to treat the regulated industry equally as though they had demonstrated materially that they share the goals of protecting public health. They have not done so.

"My second point addressed the absence of mutual understanding of what constitutes legitimate science and ethical conduct in science. The revised format does nothing to reassure me that a reasonably comprehensive understanding of Judge Kessler's extensive findings of fact in her ruling in the Department of Justice RICO case, USA v. Philip Morris, et al., is now informing the FDA's activities or has been incorporated into the agenda. These findings of fact are clearly

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relevant for the FDA to consider in its decision making, as indicated by the fact that Congress included three findings, numbers 47, 48, and 49, from Judge Kessler's ruling in the Family Smoking Prevention and Tobacco Control Act.

"While there has been a proliferation of smaller tobacco and nicotine device companies that are not defendants in the RICO case, the fact remains that the major cigarette companies continue to dominate the market, both in this country and in the world; that they continue patterns of acquisition of the more promising smaller companies, and that the federal court found their fraudulent conduct was continuing and likely to continue into the future. This is highly material to any discussion of industry-sponsored tobacco products research.

"Third, it is clear that this meeting has indeed has the effect of contributing to divisions within tobacco control, as some invitees now feel they must attend and others, including me, feel they must decline. Whether it is officially called

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facilitated dialogue or public workshop seems less important in this regard than the fact that it is still one in the same meeting with chairs rearranged and did not have to happen this way. It is disturbing when public health agencies contribute to such divisions.

"Fourth, the tobacco companies have every right to make comments, and one would expect them to do so. And the FDA has a responsibility to give comments from the regulated industry fair consideration. But legal colleagues have advised me that while the FDA is certainly permitted to invite industry speakers to present at a meeting on how to deal with industry science, there is no legal requirement that they do so; and in the absence of such a requirement, I continue to question why FDA feels it must give the industry a stage. They certainly do not have such status, even on the TPSAC where they are separated by being nonvoting members. Your legal mandate is to regulate the industry in the service of public health, not to provide it a podium for its

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propaganda.

"The leading tobacco companies have repeatedly demonstrated antipathy to the FDA, creating multiple obstacles to its ability to carry out its responsibilities for implementing the Family Smoking Prevention and Tobacco Control Act. Far from being equal stakeholders in the FDA's mission, some have sued to block implementation of health warning labels, and others are opening flouting FDA's regulations, banning the use of light and mild and other descriptors, simply replacing these words with color coding. These are only the most obvious examples.

"Our current moment does not call for a cautious, prolonged and exorbitantly expensive replay of the infamous safer cigarette debacles of the past in which the tobacco industry partnered with health researchers in a cynical ploy to buy decades' more time at the expense of millions of lives.

"What is called for now is the political courage to acknowledge and incorporate decisively

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in policy planning the vast evidence demonstrating that tobacco companies are untrustworthy; hence, the need for strong, rapidly enacted and well enforced regulations to protect the public from suffering another century of tobacco-caused deaths.

"What is called for now is informed, savvy leadership. I urge the FDA to provide it. Please enter this letter with the earlier letter to which it refers into the record of the meeting. If necessarily, I would be willing to arrange for someone to attend and read these into the record.

"Thank you for your consideration. Sincerely, Ruth E. Malone, RN, PhD, FAAN, professor and chair, Department of Social and Behavioral Sciences, editor in chief, tobacco control."

Dr. Malone asked me to let everyone know that she hopes that this is a successful endeavor.

Thank you.

MS. DILLEY: Thank you.

The next speaker is Elaine Keller.

We're not taking questions. This is not a Q&A period.

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MS. KELLER: Good morning. I'm Elaine Keller, and even though I serve as president of an advocacy organization, CASAA, today I'm testifying as a private citizen.

One of the questions to be addressed in this FDA workshop was what are the barriers to implementing third-party governance of industry-sponsored tobacco product research and how can these barriers be overcome. These questions become moot if no research is conducted, so I'm going to reframe the issue.

What are the barriers to saving the lives of smokers? After all, isn't saving lives the ultimate goal of making modified-risk tobacco products available to smokers?

One of the greatest barriers to saving the lives of smokers is the strong opinion of anti-tobacco extremists that there is no need for MRTPs. This opinion is predicated on belief in a number of falsehoods. There is strong evidence that a significant number of smokers will never be able to become abstinent from nicotine without becoming

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dysfunctional.

Those who choose to disbelieve the 2007 Royal College of Physicians' report and the 2001 Institute of Medicine report need only take a look at the adult smoking prevalence rates between 1990 and 2009 to see that the abstinence only approach does not work for everyone.

The effects of nicotine dependence are quite different from other substances. Nicotine does not cause accidents, aggressive behavior, loss of inhibition, or impaired decision making. Furthermore, these other substances can cause direct damage to the body such as liver disease, nerve disorders and dementia, whereas nicotine does very little direct damage to the body when it is delivered in some way other than inhaling smoke.

During the workshops and public hearings held by the FDA, we have seen overwhelming scientific evidence that smokeless tobacco use has a much lower risk than smoking, yet the tobacco control industry persists in publishing grossly misleading statements such as smokeless tobacco is

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not a safe alternative to cigarettes.

Research definitely shows that there is a dose response relationship between diseases and volume of smoking. Those who start smoking with smoking tend to reduce the number of cigarettes smoked when they add another source of nicotine. Many of those who completely stop smoking go through a period of dual use. Smoking reduction is proven to be an effective way for some smokers to quit, especially so when they begin to replace their cigarettes with a lower risk source of nicotine.

As long as the above myths as left uncorrected, the perception will persist among anti-tobacco extremists that there is no need to create any MRTPs. Unfortunately, nicotine abstinence is unworkable for millions of smokers. MRTPs may be the only practical solution for the millions of smokers trapped in the Sophie's choice of quit or die.

The Department of Health and Human Services needs to set the record straight. The FDA, CDC and

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NIH websites that misinform the public about nicotine and about relative risks of tobacco products needs to be revised to present the truth, the whole truth, and nothing but the truth.

In addition, since this misinformation has been deeply entrenched, the FDA needs to pave the way for public acceptance of the need for and effectiveness of substitutes for smoking by providing accurate information about nicotine, smoking, other tobacco products, and the risks of each. The FDA and other government agencies should launch a public information campaign that includes the points you see here.

In the 2000 National Health interview survey, pharmaceutical products were successfully used to quit by 0 to 35 percent of smokers, while switching to a smokeless tobacco product had a 73 percent success rate.

Let's look at the barriers to making MRTPs available. Consumers are starting to have a strong suspicion that this game is rigged. We see so much false health information about tobacco and nicotine

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spread across DHHS websites that we've begun to question everything. We have stopped taking abstracts at face value and insist on reading the entire article, and then draw our own conclusions. We have seen many journal articles where there is a mismatch between the results of the research and the way the findings are reported. And perhaps most disheartening, much of this research is funded, at least in part, by the federal government.

The requirement for extensive testing of tobacco products that we already know are lower in risk than smoking is wasteful and is a barrier to saving the lives of smokers. We have to wonder whether the bar has been set so high on purpose. Making the requirements too costly and too time consuming allows the FDA to claim that they complied with Section 911 without actually approving a single product to be marketed as a MRTP.

Anti-tobacco extremists have convinced most academics and independent companies that conduct

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scientific and health research to refuse to accept tobacco funding. Without the cooperation of these organizations, how can the required clinical trials be conducted? And even if the tobacco industry managed to conduct clinical trials without the participation of the organizations that currently conduct research for pharmaceutical companies, where would the watchdogs for third-party governance come from?

To actually save lives, FDA needs to remove the barriers to complying with the requirements for MRTP approval. To make sure that human testing can be conducted, the government needs to enlist the cooperation of universities, private research organizations, and health-related nonprofits, as well as the cooperation of other divisions of the government in getting the research done. It can only hurt public health if organizations refuse to participate in the research required to answer the most important questions. These types of projects necessarily include tobacco industry involvement. The government might give serious thought to

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refusing to award any projects at all to organizations that refuse to be cooperative.

On the other hand, the greatest threat to consumers and honest research comes from some factions of the tobacco control industry. We believe watchdogs are necessary to prevent anti-tobacco extremists from skewing the data or from reporting the results in such a way so as to sabotage the development and approval of MRTPs.

Third-party governance does not mean that tobacco industry research should be replaced with equally biased anti-tobacco research. The manufacturers should be encouraged to outsource research to independent researchers or provide third-party audits wherever possible. But they should not just allow those with opposing biases to control the research.

One way to ensure objectivity in the collection and reporting of data would be to recruit as third-party watchdogs those health and science experts who have never participated in tobacco control.

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Experience has shown consumers that we can't always trust that the tobacco control industry produces more honest research results than the tobacco industry. Let me give you a practical example. In 2009, FDA announced electronic cigarettes contained carcinogens and antifreeze. I had been smoke-free for three months when those reports were splashed across the media, and I very nearly decided it might be safer for me to go back to smoking.

The researcher Carl V. Phillips has calculated that continuing to smoke for even two more months does more damage to health than switching to a smoke-free alternative and continuing to use it for the rest of one's life. If I had not stopped smoking four years ago, by now, I might have needed to drag around an oxygen tank wherever I go.

Thank God, a few honest scientists spoke out and explained that the FDA's report was not the whole truth. Important information was left out. But how many smokers never saw the debunking

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articles and made the misinformed decision to continue smoking instead of switching? In the past four years, how many cases of COPD, lung cancer, heart attacks and strokes occurred that would have been prevented had the FDA told the public the whole truth?

Well, I guess this doesn't need a whole lot of explanation because we've already talked about the fact that we know that smokeless tobacco is a lot less harmful than smoking, so this is not true. And this message is from a fellow consumer. She's a 61-year-old grandmother and engineer who smoked a pack a day for 43 years and tried to quit six times with patches, one time with gum, a thousand times by cold turkey, and is on Prozac and is terrified of Chantix.

She says, "I finally quit this January 1st after nine months of learning to vape, learning the equipment, and investigating flavors."

I'll accept any questions you might have.

MS. DILLEY: Thank you. We're not doing any questions after public comments, but thank you very much.

(Applause.)

MS. DILLEY: All right. And our last public speaker today is Greg Conley. Is he here?

MR. CONLEY: Good morning. I'm afraid that Sharon Eubanks stole my idea for my speech, so I'm going to have to wing it.

(Laughter.)

MR. CONLEY: My name is Gregory Conley, and I am here on behalf of the Consumer Advocates for Smoke-free Alternatives Association, known as CASAA. We are the leading U.S. advocate that represents consumers of low risk smoke-free alternatives to smoking, including electronic cigarettes and smokeless tobacco and other consumers how might someday switch to such products.

We are an all-volunteer organization funded entirely by donations. Our organization does not take positions on the regulation of cigarettes or smoking, and therefore, all of my remarks should be interpreted as referring to research and regulation

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of smoke-free products and regulation about tobacco harm reduction.

Research on tobacco harm reduction and smoke-free alternatives should focus on benefitting the primary stakeholder, the consumer. Therefore, we support the principle of encouraging research that is controlled by third parties who are primarily interested in informing and benefitting consumers. However, we believe that the greatest concerns about research that is not done honestly or is done in ways that do not support the public interest do not actually relate to the tobacco or e-cigarette industries.

Recent research on these products, a significant body of which was conducted or directly funded by the tobacco or E cigarette industries, has been in close alignment with the public interest. Specifically, it has been honest research that has pursued ways to improve the health and well-being of tobacco and nicotine consumers.

By contrast, there is serious concern about

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research that is conducted and sponsored by another special interest group, the tobacco control industry, the coalition of organizations and individuals who are dedicated to the elimination of all tobacco and nicotine use. Because honest consumer-oriented research tends to support tobacco harm reduction and because tobacco harm reduction is a threat to the tobacco control industry's business model, they have actively promoted scientific disinformation about smoke-free alternatives with the intent of misleading consumers into not making the switch.

This has been documented by researchers for over a decade, and our own current research and publications document that this disinformation campaign continues. Thus redirecting some research away from the manufacturer's control and to the control of those who are specifically concerned about consumer choices and welfare might theoretically offer some modest benefits for the public interest.

To facilitate this, it is important to push

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back against the efforts to vilify any honest independent researcher who accepts industry funding, but redirecting research away from the control of the tobacco control industry would be enormously beneficial for consumers and the public interest. The worst possible scenario would be to use the principle of third-party governance of research to put more research under the control of anti-tobacco researchers who support an extremist anti-tobacco harm reduction agenda that threatens the health and welfare of consumers.

The claims that the tobacco industry engages in dishonest research are based on ancient history. Recent research conducted and sponsored by the several tobacco companies who are actively pursuing tobacco harm reduction as well as e-cigarette companies that have started to support research appears to be honest and objective science.

When someone makes claims about dishonest research from the tobacco industry, they never identify any recent example of ethical misconduct or even bad research. Instead, their claims are

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based entirely on events that occurred many years before I was born -- and I apologize if that ages anyone in the audience -- actions taken by people who have long since retired or died.

The industry's interests are not perfectly aligned with those of consumers. But the public interest can and should be served by the FSPTCA's already extensive FDA regulatory oversight. A large portion of industry-funded research can be carried out by independent researchers who are primarily concerned about consumers and about doing the best possible science. In addition, the few in-house industry research operations appear to be very interested in doing the best possible science and in considering the health of consumers, even when it does align perfectly with the maximization of profits.

Thus, we believe that the public interest could be served by the creation of some consumer-oriented, third-party institutions that conduct research that was funded by manufacturers. However, the status quo with respect to

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manufacturer-sponsored research is actually closely aligned with the public interest, and, thus, no major changes are demanded.

By contrast, anti-tobacco activists have a consistent record of publishing false and misleading claims meant to discourage would-be smokers from using low risk alternatives instead. This extends to the scientific research they conduct or control through their vast funding network.

Unlike the allegations about manufacturer opposing hidden manipulation of science, which are based on speculation and innuendo, it is easy to observe misleading research coming from anti-tobacco activists. Common tactics include suggesting that trivial risks and exposures from smoke-free products, which have no serious health consequences, are similar to the risks of smoking; denying the existence of the overwhelming evidence about the efficacy and effectiveness of tobacco harm reduction products; and, lastly, starting with the premise that tobacco harm reduction is bad and

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merely reporting that premise as if it were the result of a study.

Researchers have documented that these and other anti-tobacco harm reduction lies from tobacco control were common a decade ago, and they have increased in volume since then. Frequently, they appear in journal articles and other research papers. CASAA has a blog that is specifically devoted to identifying this misleading research that runs contrary to the public interest. We analyze several examples every week and are forced to ignore many others due to the sheer volume.

The goal of third-party governance is to take control of research out of the hands of special interests who are likely to bias the science and otherwise act contrary to the public interest. We understand that the FDA does not have any authority to redirect funds away from this misleading and harmful effort by anti-tobacco harm reduction advocates, and we would not advocate for the violation of free speech rights that such a government confiscation would entail.

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However, the spirit of third-party governance says that the FDA, and DHSS more generally, should avoid directing any additional research funding towards these activists and activist organizations. If there is an opportunity to direct research funds, whether they come from manufacturers' fees and contributions or some other source, to third parties who will do honest science that is actually in the public interest of consumers and not support an anti-harm reduction or otherwise anti-consumer prohibitionist agenda, this would probably have some benefit. However, the current research practices of manufacturers are not actually very far from this scenario.

To reiterate, the worst possible scenario in terms of public health, consumer well-being and honest science would be to transfer more research to the control of anti-tobacco activists.

That concludes my speech, and I thank you all for joining us today.

(Applause.)

MS. DILLEY: That concludes the public comment period. Thanks again to all the people who signed up for public comment.

So we'll take just a pause while we get Scott situated up here, who's our first speaker. We're transitioning now into the final segment of the meeting, which is to continue the discussion around challenges in conducting industry-sponsored research. And we begin with Scott Ballin who is a health policy consultant.

Presentation – Scott Ballin

MR. BALLIN: Thank you, Abby.

I also want to first thank the agency for the opportunity to be here today and also to extend my best to the new director of the Center who I've known for many, many years, even going back before his involvement in tobacco, so that's a long time. I also want to commend the agency for continuing to hold workshops and meetings like this, where there can be exchanges of ideas and new opportunities explored that are so important in shaping policy and decisions as we move forward, and what is to me -- and I've said this for a couple years now.

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This is a new era. As soon as FDA assumed regulatory authority over tobacco, that changed the dynamics of the discussion.

I'm not a scientist, and I'm not a researcher, but I hope to bring some perspectives to this discussion based on 30 years plus of being involved in tobacco control and public health initiatives on tobacco. And those of you who know me know that I've been advocating more recently the fact that we really do need to be focused on a more broader agenda in developing a more coherent and rational approach to regulating not just tobacco but nicotine products as well as alternative products.

There's been a sort of schizophrenia here at the agency for years with a lot of the NRTs being over at CDER, and now we have this new center. And I've written quite a bit about this. And I think we should not lose sight of the fact that this is a bigger issue than just the narrow discussions we're having with respect to tobacco.

I recognize that there are some -- and

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you've heard some of this today -- who do not think that any dialogue or engagement with the tobacco industry, as we refer to them, is either appropriate or beneficial, even in the scientific arena. And one such critic recently told the Washington Post, the industry is not a stakeholder. And I respectfully disagree and think that this is in this new era of regulatory oversight -- we now have the opportunity to ensure that the industry's behaviors will never be repeated.

The Chinese general -- and I think many have heard this expression before -- made the comment that "Keep your friends close and your enemies closer." And I think this is a perfect example where we need to be watching the industry on a regular basis, involving them directly in discussions. I'm not talking about negotiations. I'm talking about actually face-to-face dialogues such as this meeting that's taking place.

I think the IOM was correct in its report to raise awareness that based on the industry's past behaviors, there's reason to be wary and cautious

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as we move forward, as their past actions have, quote, "Resulted in significant distrust of the tobacco industry."

Yet at the same time, the IOM recognized it will be the manufacturers, broadly speaking -- and again, I'm not just talking about traditional tobacco manufacturers -- who will have the burden of producing scientific evidence about the MRTP products that will be developed and produced. And so their involvement is obviously going to be required and essential in this process.

After raising the yellow flag of caution -- or maybe I should say a red flag -- the IOM goes on to say, "Regulatory policies also should seek to promote the meaningful involvement of stakeholders that include the tobacco industry, academic researchers, public health advocates, and the public as well." That includes consumers. And I would suggest that the statement be broadened to be specifically inclusive of any manufacturer, traditional tobacco companies or others -- it may be a biotech company; it may be a pharmaceutical

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company -- who seeks approval from the FDA for an MRTP.

Along those same lines, I want to point out that it's no longer so easy to define the tobacco industry as well as the use of the word "tobacco" as it was in the '70s, '80s and '90s, and it will become increasingly difficult to do so. We need a serious reconsideration of the terms that we are using. The focus should be more on the science and also on the products that are being developed and less on who's making them. I mean, we could get rid of the entire tobacco industry and still have a lot of chaos out there. We have to begin to break this down and approach it differently.

It's not again just about tobacco. It's about nicotine products as well. It's not so inconceivable that a pharmaceutical company, a device company, a biotech company will produce an MRTP, or even a food company that deals with agricultural-based products and science on a regular basis who might apply its technologies into developing and producing an innovative very

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low-risk product. That's very feasible.

Traditional tobacco companies are themselves expanding their portfolios that include a spectrum of tobacco, nicotine, and alternative products. So we have to begin to think outside the box a little bit as we have these kinds of discussions as we move forward.

I also believe that had the Institute of Medicine had the time and had not been constrained by some of the requirements within the statutory mandate, that the report could have been further enhanced by making site visits to all the tobacco companies who they were concerned about and raising red flags about to gather more information, that may have actually helped in the process of putting the final report together. And I think that was a missed opportunity, and that is again why I think there needs to be more engagement, and not just from this agency, but by all interested parties in reducing harm caused by tobacco.

So the IOM was, to me, also very correct when it stated that the committee was particularly

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wary. And this was, to me, one of the most important statements of the report, even though there's so much in there. They were wary of making perishable recommendations that may lose relevance as time passes and scientific methods and technologies evolve.

And that's where we are. We're in this new era where we don't know where we're going and what's going to happen. It is very clear to me that by having these kinds of dialogues, we can shape where we go. We can prevent problems of the past. And we can see science evolve that is going to develop new products that actually will do what public health goals should be, and that is to reduce disease and death caused by tobacco.

I also believe -- and this has come up the last couple of days -- that the FDA has a major role in helping either to do the third-party governance or providing the mechanisms to be able to bring people together to do it. And that should be explored on a continual basis. There should be a follow-up meeting to this workshop where that

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could be discussed on what that should look like, and I would hope that that would happen.

Just a few comments that I think need to be incorporated, that any oversight must be of the highest ethical standards. There must be transparency -- you've heard transparency mentioned over and over -- across the board. And every effort should be made to minimize conflicts of interest and interference. The development of fair, consistent and uniform regulation and standards that are applied to all entities seeking approval of MRTP is essential. And there must be continued open lines of communication. And as I said before, the IOM correctly noted that some flexibility is going to be needed to deal with evolving technologies and scientific methods.

Manufacturers, researchers, research institutions and others should be a part of the process by and through which the standards are developed. And I think excessive regulatory and even scientific bureaucracies that impede progress in moving things forward should be avoided but

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without sacrificing proper oversight.

Public and private engagement of all stakeholders for the discussion of science-related issues in a neutral safe forum should be encouraged, not discouraged.

FDA should be commended for its leadership role in advocating dialogue, and I strongly believe that it should not retreat or back away from a more transparent approach due to outside pressures. People want to participate; they participate. If they don't want to participate; they don't participate. But transparency and discussions, in my view, are absolutely important.

Justice Brandeis, famous saying again, "Sunlight is the best disinfectant." And if we can shine a light on the tobacco industry, and bring them to the table to have dialogues and discussions -- and, again, I'm not talking about negotiations -- we can move this ball forward in a much more significant manner.

I've been proud to be a part of the University of Virginia's Institute for

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Environmental Negotiations that has held a series of dialogues on tobacco-related issues. The first ones they did were in the '90s and brought public health and growers together. They have a track record of success. They have started some new dialogues, and I commend them for doing that. The focus is on harm reduction issues, not on trying to placate the industry or do anything like that, but rather looking at the need for new policies related to tobacco, nicotine and alternative harm reduction strategies.

They produced a set of core principles in 2011 on issues related to corporate funding for tobacco, nicotine and alternative harm reduction, which could help guide and stimulate further discussions in the public and private sectors. I will be submitting that on their behalf for the record, but I'd like to sort of highlight a couple of the things that were mentioned.

Recognize and accepted, that it should be a shared goal of all parties to reduce disease and death caused by the use of tobacco; that science

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should be used to assist the regulatory body in setting the standards on how a spectrum of low risk products should be labeled, sold and marketed.

That an independent third-party regulatory authority such as the FDA is essential for overseeing and setting fair, workable and effective regulations designed to achieve goals that were outlined in that first bullet that I mentioned about a shared common objective.

That academic research institutions have in place and promote publicly available conflict of interest policies that prevent or limit the funder, the research institution, the researcher from misusing or distorting the purposes of the research for which the funds have been allocated. Such research should -- and this was a very important component of this -- have a public health objective. So it wasn't just general research that went nowhere. It had to have public health goals.

That consideration should be given to the development of models that can be used by research institutions to establish the necessary safeguards

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that will ensure the highest integrity of the research being conducted.

I also wanted to mention as I listened yesterday about -- someone had said there was limitations on the number of universities and academic institutions receiving funding from the tobacco industry. There's probably more than were mentioned yesterday, but I also want -- Dr. Ashley will know that I'm going to raise an agricultural issue because there is a tremendous amount of research going on in land grant colleges and also other universities looking at the tobacco leaf.

My view is, is that the tobacco leaf is going to play a very important role in the development of modified-risk tobacco products, particularly the noncombustibles, because that is where you can remove the nitrosamines, reduce the heavy metals, and do other things to the tobacco that could actually have a very important impact, public health impact, on users of those products.

So I don't want them to left out. I know you don't have jurisdiction over that area, but

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it's important, I think, to be able to look at that from the broader perspective and start working with USDA and others on those issues.

I wanted to leave you with a quote that was made by former Commissioner David Kessler about 15 years ago at the conference that was sponsored by FDLI and Georgetown University. And he said, "I hope that someday the industry scientists would be able to talk in a public forum about what they have known and what they have learned about nicotine administration over the years."

Well, I think we're there. We're at the beginning of that process. I encourage all the various interested parties and stakeholders to get themselves involved, be transparent. Industry should be opening its doors and inviting researchers to come and inspect the research facilities and their agendas, not have a closed-door policy.

So there's a lot to be done, and I commend the agency for holding this meeting today and look forward to future meetings. Thank you.

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(Applause.)

MS. DILLEY: Similar to yesterday with the panelists, we'll take a couple of questions.

Can you introduce yourself and wait for a microphone? Again, we have people online, so.

MR. ROSE: Jed Rose. Thank you, Scott, for that characteristically reasonable and balanced summary. I was wondering if you see an analogy -- you talk about the new era, and there's been off and on discussion of history, one speaker pointing out that often the tobacco control community, some members of the tobacco control community, have rehashed over and over the ancient history, and history is continuing to evolve.

But do you see an analogy -- I remember learning in high school that when the Revolutionary War was fought with Great Britain that early on it was very helpful to have very strident rebellious activists like Patrick Henry, but then once the war was won, it took the likes of Benjamin Franklin and George Washington and so forth to craft the Constitution and actually make progress with the

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new society and getting work done.
Do you see an analogy now that we are entering a new era where really constructive collaboration has to be the mantra?
MR. BALLIN: I do, and I think our history is full of examples like that. I mean, you can look at the wars with Germany over the years. Do we still treat Germany as an enemy after having two miserable wars with them and the Japanese and everything else? Soviet Union, another example. I mean, there are tons of them out there, of examples where something happens that changes the debates and discussion, and I think that's what's happened here.
It's hard to let go. I'm part of all of that era, that beating up on the industry, and I still will; I will continue to do that. But I also see an avenue here where instead of fighting the war and just lobbing bricks over the wall at each other, I think that by having meetings like this that are controlled, where people don't dominate it, one segment versus another, that we can

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actually have some discussions to move it forward.
It may be only a few things that move forward. There may not be much agreement on some stuff. But I have learned by my own experiences with working with the growers and working through this kind of a process that you don't know what to expect until you've actually sat down face-to-face with people in a safe environment and started some sort of a dialogue.
MS. DILLEY: Are there any other questions?
I think, too, that some of the discussion is focused on what are the criteria. I mean, there's part of the history, but there's also what are the criteria to get us to credible research. And there was a lot of discussion yesterday about independence and transparency, so what does that look like in going forward.
Because I think your point, Jed, to some degree is so how do we move from where we are to where we need to go. And I think there was a lot of discussion of that yesterday, and hopefully we'll continue that today, focusing on what does

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that mean concretely, what does that look like, transparency and independence.
David.
DR. ASHLEY: David Ashley, FDA. Scott, I was just very interested in one real small aspect of your slide. I wonder if you could help clarify it.
You talk about the process needs to be consistent and flexible. And I find that very interesting. I'm just wondering if you've got some good examples of a system that's consistent and flexible.
MR. BALLIN: I think that, for me, setting out broad principles that show consistency of a policy development but being able to be flexible if something changes. My own experience is that I could say that we'll carve everything in stone, and we won't deviate from it. That's consistent, but it's also unflexible because if I set out 10 standards or 10 recommendations and say, this is what we think we need to achieve, there's got to be some flexibility about working within that system.

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Does that answer your question?
MS. DILLEY: You're looking for a specific example --
DR. ASHLEY: Yes, that sounds -- I understand the principles and everything. The problem gets to be when you actually have to make regulatory decisions based on that, and I'm very interested in whether the industry wants us to be consistent or flexible. The word I've gotten is we need to be consistent, and then other times depending on the situation, they want you to be flexible. And so it's always an interpretation. It's just not an easy balance to achieve, particularly in a regulatory agency.
MR. BALLIN: Yes, I agree with you a hundred percent. And I think that that's why these kinds of meetings are actually very important, because you can actually develop some consistency about where you need to go, some sort of direction that everybody might agree to. But then that roadmap is going to change as things change, and that's -- it happens in life all the time.

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It's just not in a regulatory agency, but things happen in our lives that we don't predict, that we cannot control, even though our best interests are to have some consistency in what we want to achieve. I mean, I think we all make decisions every single day that we wanted to do something, and something got in the way and we had to change the direction.

I think that the regulatory agency has to be flexible enough, and I think that's what the IOM suggested in a couple places in there, that we can't put these recommendations in stone because they're perishable, and we must be wary because of the evolving science and technology. And I think the FDA needs to take the same type of approach, even though it wants some consistency and direction about where it needs to head.

MS. DILLEY: One more question, and then we need to move on.

MR. DELMAN: Hi, Scott. I really enjoyed your comments this morning, as I generally do. Farrell Delman from TMA.

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I'm wondering if you had a chance to listen in on yesterday's conversation where we discussed quite a bit the IOM recommendations, and there was a number of comments associated with Recommendation Number 10, particularly, and concern among some of the people here that preapproval of third parties is a recommendation they could not support. And I think the sense was that such preapproval of third parties might lend itself to violating in some sense the overall objectives of the independence of third-party governance.

I guess I'm wondering if you've got any thoughts at all on Recommendation Number 10 and the conversation that we had yesterday.

MR. BALLIN: You know, Farrell, I don't because, as I said, I'm not a scientist or a researcher, and there are a lot of issues that go with that. But what I would say is that's a perfect topic for further discussion here at FDA and outside of FDA, because if people were to sit down and maybe work through some of these things and issues, maybe something could be developed that

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is more acceptable by a broader spectrum of people.

As I said, the thing that I learned in talking with farmers is there is so much misinterpretation of people's views, and until you have them in the same room, and you ask them a question, and you have a dialogue about it or discussion and get clarification, all you're doing is polarizing the process. And I don't think we are at a point here where we want to polarize process anymore because we're in a regulatory environment, and we've got a lot of different stakeholders, and we've got different products being developed by a broader spectrum of people, so we need to think differently.

MS. DILLEY: Thanks, Scott, and you'll be able to come back up at the end of this panel and provide some more responses from our Q&A.

We need to move to our next presenter who's Donald Graff, who's a clinical research scientist with Celerion.

Presentation – Donald Graff

DR. GRAFF: So I think I'm going to switch

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directions here pretty significantly. Yesterday, we also had a presenter who's working from the trenches, and I sort of see myself in that regard as well. So as the sign says, my name is Don Graff, and as a clinical research scientist at Celerion, part of my job is to design studies and write protocols as well as analyze and interpret data and write clinical study reports for our tobacco sponsors.

For those of you who might be unaware, Celerion is a contract research organization, or CRO, that focuses primarily on conducting early phase clinical research studies for pharmaceutical companies. However, over the last 12 years and including under our previous name of MDS Pharma Services, we have performed clinical conduct, analyzed data or analyzed biological samples for more than 50 studies for tobacco companies.

So it's with that experience that I understand that the development of modified-risk tobacco products is going to be an effort that will benefit from the expertise of individuals in areas

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such as academia, public health, and government and, of course, the tobacco industry itself.

So I'd like to start off with just highlighting a couple of benefits that I think that CROs could bring to the table in this regard. On a high level, areas of essential expertise that I think the CRO industry does bring to the table include working with good clinical and laboratory practices and regulatory submissions. And it's because that we live in this GxP and regulatory environment day by day, in my opinion, there's no better partner that a tobacco company could have than a CRO when it comes to performing this work to meet ethical, scientific, and regulatory demands that are going to be necessary.

So the advantages then of working with a third party adept in best practices and industry standards is getting better, cleaner data to the FDA, which I'm sure that they appreciate, or we've come to know that they appreciate clean data, more quickly and at a lower cost. And similar to our pharmaceutical work, there are going to be

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successful products and unsuccessful products.

So the primary concern that I have is only that we provide a high quality deliverable at the end of the project or program, and, of course, we always hope for the best outcomes for both our pharmaceutical and tobacco sponsors. But we often have to remember that success can also be defined as getting a failing or harmful product out of the development chain as soon as possible.

So at the project level then, experience and expertise that can be found in a CRO can specifically help with the public perception issue that exists and help to reduce the potential for bias in study design, statistical analysis, and data interpretation of a tobacco trial, just as it can in our relationship with the pharmaceutical industry.

Because we are looking at new product applications as the end product here, in my opinion, no other group has the capacity to conduct the number of trials, recruit the number of subjects, and analyze the mountains of data that

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are going to be needed to bring new products to market in a timely manner.

So on the next few slides here, I touch on some of the high level challenges that we face in general when it comes to conducting tobacco studies. As you can imagine, there are a number of operational and logistical challenges as well with any clinical trial or a set of clinical trials, but I'm not going to go into a lot of specifics in these remarks.

The first of the challenges that I would like to bring out, in my opinion, is the most significant challenge that we have, is how do we meet the FDA's requirements and expectations. I do commend the FDA for the guidance that they have been able to put into place so far, but from an operational standpoint, these guidances primarily provide high level direction. And from our perspective, there are a number of specific details that are yet to be determined.

Looking to the pharma industry, for example, when it comes to early phase research, I can find a

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guidance document on just about every study that I would need in order to move a drug through the development process. So my hope is that the FDA follows this model and expands upon the information that is in the current guidance and perhaps provides some sort of formal framework to bring a product to market.

So with regard to what we can take from the guidance documents that are currently available, in my opinion, the exposure studies and most of the health risk evaluations for tobacco consumers that are going to be required are relatively straightforward. But it's the requirements for the evaluations of non-consumers' perception-type studies and post-marketing studies, especially, where companies in our industry might need to call upon experts in other areas for their expertise.

For example, evaluations that include adolescents and other vulnerable populations that were mentioned yesterday, according to the regulation, these evaluations need to take place in order to get a product approved. So somebody's got

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to carry them out, but who? If we are to be involved, we in the CRO industry are going to either have to adapt our services or call on experts in academia or public health to help with items such as this.

Next, statistically, what is going to be the burden of proof when it comes to demonstrating success or failure, and how do we define appropriate for the benefit of the public health? Will a definition of clinical significance need to be determined for various evaluations, or will a simple statistically significant finding be sufficient?

With regard to how the introduction of a new product into the market will affect things like cessation or initiation, will any decrease in the cessation rate or increase in the initiation rate be acceptable, even if overall exposure to harmful or potentially harmful constituents are reduced? And when it comes to evaluating these HPHCs, are any more critical than others? So what if some constituents go up slightly and others go down?

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These are just a few of the more basic questions that we have had when reading the guidances, and it would be very helpful if these kinds of questions were considered in future guidance documents so that we can design studies appropriately.

Then to the last bullet here, how do we balance the benefit to individuals to that of the population of the whole? Certainly, public health should be considered and the burden of proof should be set very high, no doubt, but not so high that it's impossible to approve reduced risk products that could replace more harmful products, thereby eliminating the benefit to consumers who wish to use them.

So next, there's some site selection and challenges in facilities' needs that need to be dealt with when it comes to conducting tobacco studies. As we've been evaluating our need to develop clinical partners for this work, we've found that few states have clear language within their tobacco regulations that provide clinical

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research exemptions for combustible product use indoors. And as these cigarettes become more and more popular, more and more states are also including them in their indoor smoking bans as well.

So based on my very non-expert interpretation of the state laws in all 50 states -- I'm a scientist and not even close to having the legalese when it comes to evaluating or interpreting laws. But according to what I've seen, there's only 14 states where it appears to be clear that we can conduct in clinic evaluations of combustible products.

This, of course, makes it much more challenging to meet the regulatory requirements, as it is clear that even for new noncombustible products, evaluations will need to include comparisons to conventional combustible products as well.

So when we do identify states where the work can be performed, we need to find facilities that are equipped to actually do the work, as special

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processes, procedures and SOPs must be put into place to carry out the activities are required for evaluating tobacco products. For example, does the facility have an adequate ventilation system that isolates air flow from rooms where smoking occurs so that it is not redistributed to other sections of the facility?

To go along with that, there are staffing considerations and investigator qualifications that also need to be considered. At Celerion, for example, we do not require our nonsmoking staff to participate in clinical conduct events where smoking takes place. And in addition, due to the very low limit of quantitation for nicotine that we have in our bioanalytical lab, we also can't allow staff members who smoke or use tobacco products to perform some processing steps so that we can avoid contamination of the samples. So appropriately staffing these studies can also be a challenge.

So next are some ethical considerations. Obviously, there's more ethical considerations than what we can discuss here in the time that I have,

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but these are some of the items that we're looking at currently.

An important consideration here is how do we fully understand new products without encouraging or increasing their use. Obviously, we don't want to introduce a product to someone who otherwise may not have considered trying the product, such as adolescents and other vulnerable populations.

Also, at the project level, clinical trials require subject compensation, and sometimes study products are provided to subjects free of charge during the study. So this can be problematic, as it may be perceived that subjects are being coaxed into trying something new. Hence, we are very careful when we create the inclusion and exclusion criteria for these studies and determine compensation rates in order to minimize any ethical issues and operational problems that might arise in the face of this free product effect.

This next bullet might also be considered an ethical matter for individuals called on to do the work, and that is, as a healthcare professional,

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how do you justify working on tobacco products? For me as a former and sometimes current practicing pharmacist, it's not a question that I struggle with anymore, especially when I keep in mind that the goal here is to reduce tobacco-related morbidity and mortality by bringing less toxic products to market. If we're able to reduce from the 440,000 deaths that are attributed to smoking each year in the U.S. by significantly reducing exposure to toxicants, then we have achieved that goal, in my opinion.

Also, there's a significant need for education regarding how tobacco product research and healthcare align. We're all familiar with the burden that tobacco has put on healthcare as well as the benefits, or the potential benefits, that might come from modified-risk tobacco products. But in order to make this work rather than dwelling on the past, we need to focus more on what we can do to conduct this research to the highest ethical and scientific standards going forward. And at Celerion, we feel that we do this with each and

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every study that we work on with the highest integrity.

So we might find ourselves, for example, educating the IRB or ethics committee, facilities, vendors, other subject matter experts that we might call on as the needs arise, especially if they have not been involved in such studies in the past.

Lastly, even the Pharma-CRO model has its limitations and drawbacks when it comes to being an all-inclusive partner in this. While there are many similarities to our pharma work, there are numerous operational and logistical details that need to be taken into account with this kind of research. So significant pharma experience does not necessarily guarantee success in this market space.

Also, because of some of the special requirements of this work, there may be gaps in the current expertise and facilities available within CROs currently that need to be filled either internally or by partnering with external subject matter experts. So not all CROs could provide

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comprehensive program oversight on their own. However, I firmly believe that if a CRO wants to contend in this space, that it will find a way to fill those gaps.

Finally, and I think very importantly, considering the overall topic of the workshop here today and yesterday, bias and preconception may be minimized with a model that closely follows the Pharma-CRO model, but no model or governance structure will ever be able to completely eliminate them. So just as there may have been indiscretions in the development of pharmaceutical products in the past, we also run the risk in this area of research. So all stakeholders must remain vigilant to keep this work to the highest ethical and scientific standards.

Finally, just a couple of concluding thoughts here. I'd like to note that we must not forget that the objective of MRTP approval is to provide safer products for consumers who wish to take part in a legal activity and that the Pharma-CRO model would provide an excellent

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starting point to provide independent third-party oversight of tobacco-related research.

Thank you.

(Applause.)

MS. DILLEY: We have time for one or two questions before we take a break, questions or clarification.

MS. GAGOSIAN: Hi. Stacey Gagosian with Legacy. I'm not familiar with the pharmaceutical approval process.

Do you-all contract directly with the sponsors, or do you go through FDA?

DR. GRAFF: So almost invariably, we contract directly with pharmaceutical companies or biotech companies. On occasion, especially when we work with some of the small biotech companies, we might contract with a third party who's sort of overseeing their development. But, typically, we don't directly work with the FDA. I mean, we obviously have a lot of interaction with the FDA, but not from a contractual standpoint.

DR. BACKINGER: Good morning. Cathy

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Backinger, Center for Tobacco Products, FDA. You mentioned in your slide on ethical considerations around youth -- and obviously, of course, there are ethical considerations. But through NIH and other federal agencies, there's been research conducted with youth around perceptions of tobacco products, following kids over time to see if they initiate or start.

I'm wondering, does your company do work with youth from your other work, or is that -- what is your policy in that regard?

DR. GRAFF: So historically, even with pharmaceutical products, we haven't done a lot of work with children, adolescents, in that regard. It had a lot to do with the IRB that we used to have as MDS Pharma Services. They just weren't comfortable reviewing, for the most part, work with children. So we've sort of avoided that. In that tobacco area, no, we have not done any work with adolescents or youth of any kind.

Typically, when we're designing our studies, the inclusion and exclusion criteria require

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subjects to be at least 19 years of age in Nebraska for the studies that are run there, and usually, they're even a little bit higher because of some smoking history requirements that are also considered in some of those studies.

DR. BACKINGER: And just looking at your concluding thoughts, your first bullet about consumers who wish to take part in legal activity, research over the past many decades show that most adults -- 87, I think, percent of adults who smoke started smoking before they were 18. And the statute dictates that we need -- that a sponsor of an MRTPA need to take into account both users and non-users, including vulnerable populations such as youth. So it's an important consideration.

DR. GRAFF: Absolutely. And I can tell you that, again, as we evaluate external clinics that we might work with to conduct some of this research, I can tell you that in some cases, those independent clinics have done smoking cessation work and evaluations with adolescents. So when I say specifically my company has not, it doesn't

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mean that some of the other clinical facilities that we have had talks with don't do that work. And, of course, it is very important.

MS. DILLEY: Okay. I would like to take a break now and come back at 10:15. Donald will have a chance to respond to additional Q&A when we get to that point in the day. So we'll start right back up at 10:15.

(Whereupon, a recess was taken.)

MS. DILLEY: So we wanted to keep pretty much on time because we do have a series of five speakers for this next stretch, and then we'll move into Q&A with all the panel members, so that will be seven people.

Next up is Lars-Erik Rutqvist, who's the senior vice president of scientific affairs at Swedish Match.

Presentation – Lars-Erik Rutqvist

DR. RUTQVIST: Thank you, and good morning. I'd like to start this presentation by noting that research governance is not a new issue, nor just a tobacco issue. There are several product areas out

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there that have governance structures implemented more or less successful. And although tobacco is different, not least because of the public health provision and the Tobacco Control Act, and therefore requires extra scrutiny, it is reasonable that the establishment of an infrastructure for tobacco builds on the experiences that FDA has from other fields. And so it's natural that the Center for Tobacco Products provides leadership in this development.

With that said, it's equally important that industry and other stakeholders are open minded and are willing to change and contribute thoughts to the process because, otherwise, if you're not interested in a dialogue around these issues, you run the risk of becoming irrelevant to the process.

The chapter on governance in the IOM report was not surprising. Now, whether you agree with the conclusions or not in the chapter on governance, I think you have to accept that it accurately reflects how the tobacco industry is perceived. But I don't think that considerations

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related to the troubled past of the U.S. tobacco industry should make us lose sight of what's important today in this new era of the Tobacco Control Act. And I'd like to quote from the report that, "Establishing the tobacco industry as a legitimate participant in tobacco research is an important consideration in the overall goal of producing evidence on the effect of modified-risk tobacco products."

I only wish the IOM committee had offered a more defined path forward to the establishment of a comprehensive research governance structure for tobacco, but that was perhaps beyond the scope of the committee's charge. And so I think it might be a good idea to appoint a new committee to provide the necessary follow-up.

I think we should also be aware that there are governance models out there to consider, and my Swedish Match colleague Jim Solyst recently wrote an article for the FDLI journal named, Will Public Private Research Partnerships Improve Research Funding and Application? And I know there are some

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hard copies of that paper outside this conference room, and if you can't find them, please approach Jim during the break. I know he has some hard copies, also.

I'd also like to acknowledge the initiative taken by a group of tobacco researchers a couple of years ago. They met to explore innovative funding models for tobacco research, and we heard Joanna Cohen elaborate on this initiative yesterday.

In order to be realistic, I think we have to accept that it will take time to establish a comprehensive governance infrastructure for tobacco. But research on MRTPs cannot wait. Since the Tobacco Control was passed in 2009, there's been a significant increase of research articles on this subject. And I don't think that this momentum should be slowed by these deliberations about how the research governance infrastructure should look like. In this context, it's important for industry to be aware of this issue and contribute thoughts as to how the process can be approved.

Yesterday, we heard about models for how

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third parties can assume key functions of research governance such as funding, setting research priorities, and actually doing the actual research themselves. But companies have a -- the Tobacco Act requires product-specific research when it comes to modified-risk products, and companies because of their product stewardship commitment should also do research. And I think there are examples of the types of research that it would be very difficult for third parties to assume key functions of governance. And I think a good example of that type of research is the development of the GothiaTek standard for snus products. That standard was developed by Swedish Match. It originated as a collaboration between toxicologists at the Swedish Food Authority and the company, but the continued research required to develop the standard was done within the company. And it was based on an intimate knowledge of all parts of the manufacturing process. And I don't really see how a third party really could have contributed to that research effort. So I think product-specific

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research should be both a corporate obligation, but with the Section 911, it could also be a competitive necessity.

The MRTP process requires product-specific evidence, and therefore, it's in the best interest of companies and public health that this research proceeds in a timely manner. And I think the conclusion that I'm getting at is that before a comprehensive governance model has been codified or mandated, companies must institute their own research governance.

As an example, let me mention the clinical trials with snus that Swedish Match has sponsored in recent years, and these studies were initiated well before the Tobacco Control Act was passed. I won't go through all of these bullet points, but let me just say that even though there was no Tobacco Control Act, we were aware that credibility of the evidence was a key issue. And in order to ensure credibility, we thought the best idea was to institute proper governance of the trial, and we more or less emulated the pharma model for

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governance but added a few extra features.

Let me just highlight where we involved third parties. For instance, the protocols were developed not by us, which is sometimes the case in pharma trials, but they were a collaboration between the individual research teams that did the research and Swedish Match. Also, we used contract research organizations to be responsible for all data handling, data monitoring, and statistical analyses according to prespecified statistical analyses plans.

We registered the trials in public databases such as clinicaltrials.gov. And finally, already at the outset, we made a commitment to publish the results of the trials irrespective of the outcome. We also made a commitment to make individual patient data from the studies available for systematic reviews and meta-analysis. I'm sure you're aware that this is something that pharma companies sometimes have been criticized for not doing.

Now, implementing a governance structure

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such as this had its challenges, and I won't go through all of them. But just let me mention that there are some IRBs or ethical committees out there who consider all studies involving tobacco uses as inherently unethical unless they aim at total tobacco abstention. And, of course, that type of position is not consistent with the research on modified-risk tobacco products, and, unfortunately, we lost a number of centers because of this problem.

Also, recruitment of CROs can be a problem. I found that some CROs in this country have a policy of not working with tobacco companies, policies that sometimes are explicit, and sometimes you find out after a while that they are not comfortable working with a tobacco company or with a tobacco product.

Also, for CROs that are willing to work with a tobacco company, there are a lot of challenges, and I think the gentleman from Celerion very adequately presented some of the problems for a CRO to work with a tobacco company and with tobacco

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products.

The third bullet point is not relevant for studies conducted here in the United States, but internationally, it can be challenging to perform studies with a tobacco product where there's no traditional use of the product category. Just getting it over the border can be a difficulty.

In some countries, there are regulations that state that all clinical trials must be approved by the Medical Products Agency. And to have such an agency approve a trial with a tobacco product can be quite challenging.

As transparency and external oversight are central components of any successful governance structure, Swedish Match has decided to take a further step when it comes to research related to MRTP products. And so I'm delighted to be able to make it public today that Swedish Match has initiated an external independent advisory panel on matters related to research and analysis for modified-risk tobacco products.

The founding member of the panel is

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Professor Karl Fagerstrom. It was natural for us to turn to him because we worked previously on the clinical trials, but the other members of the panel are U.S. based and represent the broad range of relevant science areas; for instance, risk communication, toxicology, research ethics and, of course, tobacco research.

Now, I'd like to emphasize that I cannot speak on behalf of the panel because it is an independent body that will develop its own mission statement, and the members are free to raise any relevant issue. But just let me mention that the panel's deliberations will be guided by the public health interest. There will be no contractual or confidentiality agreements between the company and the panel members. And I know that the panel would like its activity to serve as a model for how a tobacco company can interact with an external science-based group.

The inaugural meeting was held just a few weeks ago, so this is a completely new panel. It's evolving. So what the eventual outcome will be of

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the panel's activities, obviously, is difficult or even impossible to predict today. But, obviously, we're all very excited to work on this initiative.

So, in conclusion, I think that comprehensive tobacco research governance infrastructure is badly needed, and the Section 911 of the Tobacco Control Act is a potentially powerful tool to achieve this. I think that the CTP should continue the types of dialogues that are exemplified by this workshop, and I think also that CTP should consider funding an IOM committee charged with elaborating on the ideas in the governance section of their recent report.

But we should also be aware that governance is a long-term project, and in the meantime, research must continue. And companies like Swedish Match need to establish their own governance provisions.

Thank you.

(Applause.)

MS. DILLEY: We can take a couple of questions.

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MR. APELBERG: Ben Apelberg, Center for Tobacco Products, FDA.

I just had a clarifying question for the point you mentioned about the commitment to make individual study data available. So does that include sort of availability to independent academic researchers who would want to analyze it and publish a systematic review or analysis? And if so, have you thought about a process for making that available, and have you actually done that yet? Or is this sort of talking about a principle that you intend to put in place?

DR. RUTQVIST: Well, the answer to your first question is yes. The trials have been published. So far, we have received no requests for making access to the data. We've also done a systematic review and meta-analysis of the trials. That paper was recently accepted for publication. Perhaps that will stimulate the interest in the trials and will sort of make people aware of the fact that you can do that. And if we receive such a request, we will definitely make the data

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available.

MS. DILLEY: Other questions?

DR. HUSTEN: Corinne Husten, CTP. I just had a question about the advisory panel that you're setting up.

Will those meetings be like open public meetings?

DR. RUTQVIST: That is something that the panel would decide. I don't know.

MS. DILLEY: So they're structuring their own governance?

DR. RUTQVIST: Yes.

MS. DILLEY: Matt?

MR. MYERS: Thank you. That was interesting.

MS. DILLEY: Can you introduce yourself?

MR. MYERS: Sure. I'm Matt Myers with the Campaign for Tobacco-Free Kids.

I've heard you and your colleagues speak before and speak pretty glowingly about the research done on the GothiaTek method, and you highlighted that there as an example of a kind of

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research a company should be doing; and heard you previously talk about the belief about the low level of disease risk of products that meet the GothiaTek standard with regard to that.

So I guess my question is how that translates. Do your products in the United States meet the GothiaTek standard? And while your presentation focused on Section 911, if, in fact, GothiaTek standard was shown to be significantly less hazardous than even other smokeless tobacco products, would you support a Section 907 product standard so that everybody is protected by that?

DR. RUTQVIST: You should know that the GothiaTek standard is a product standard for snus, and it's a comprehensive product standard that doesn't only include the maximum levels of certain selected toxic compounds. It's a standard for production technique, for qualified consumer information, which, obviously, we can only implement outside of the U.S. at the moment.

MR. MYERS: But there's no technical reason why you couldn't in the United States.

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DR. RUTQVIST: But all snus products sold by Swedish Match here in the U.S. adheres to the GothiaTek standard, but I'm sure you know that Swedish Match also manufactures American moist snuff products. And we worked over several years to make them comply with the maximum levels of these potentially toxic compounds that are covered by the standard, and we've come quite far with that.

But because of manufacturing differences and the obvious product differences, there are a few of these compounds that we still don't meet the GothiaTek standard. But I think if the GothiaTek standard, which is at the moment a voluntary standard -- if it were accepted, I think it would be an enormous competitive advantage to have products comply with the standard. So I think you would see a development for many products towards that goal, if it were accepted.

MR. MYERS: I'm confused. Just pure point of clarification. In Sweden, all products, all non-combusted products that you sell meet that

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standard. Am I right about that?

DR. RUTQVIST: All snus products in Sweden and in the U.S. manufactured by Swedish Match meet the standard.

MR. MYERS: But in Sweden, do you make any other smokeless tobacco products?

DR. RUTQVIST: No.

MR. MYERS: No. And so I guess my question -- in the literature I've read, you've all talked about one of the reasons for that is the government has set that as a standard because of health and safety concerns. And so I guess what I'm asking is, if it's good enough in Sweden, why don't we do it in the United States?

DR. RUTQVIST: You should ask that question to the CTP, not to me.

MR. MYERS: But what I'm asking you is with Swedish Match, would you at Swedish Match support not just a 911 exception but support that all smokeless tobacco products meet that standard?

DR. RUTQVIST: Yes.

MS. DILLEY: All right. Thank you very

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much. And people will have a chance to ask Lars-Erik more questions when we have the Q&A for the full panel.

So next we have Michael Ogden who's senior director of regulatory oversight, RAI Service Companies, R.J. Reynolds Tobacco Company.

Presentation - Michael Ogden

DR. OGDEN: Thank you. Good morning, ladies and gentleman. Mike Ogden, RAI Services Company. I'm here on behalf of CTP-regulated tobacco operating companies under the RAI operating family. It includes R.J. Reynolds Tobacco Company, the American Snuff Company, and Santa Fe Natural Tobacco Company.

Just a brief outline of my comments this morning. I'll start with a few key takeaways. Give you our view of the transformation that's going on in the U.S. tobacco industry. We believe that we are championing that effort. Talk briefly about some issues and opportunities with third-party governance. And for that conversation, I'll frame it in light of a couple of the IOM

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recommendations. And then we'll talk about some key conclusions.

One point I'd like to make clear -- and I was in the audience yesterday, as many if not most of you were as well, and there seemed to be a bit of conflation of the different types of research that might be -- that will be required under a modified-risk tobacco product application. I don't know if that was intentional or perhaps even desirable, but basically as I sat and listened to those comments and the discussions yesterday, it was often unclear as to which piece of the research one was speaking about.

I easily see three areas of research relevant to modified-risk tobacco products. There's the development of research tools that could be used broadly across any potential modified-risk tobacco product. There's also the product-specific research that's required to support an application, and then there's obviously requirements for post-market surveillance, both in development of tools and also the implementation of

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those research tools.

So I thought it was a useful comment to put that in front of you, and then to say as a preamble to my comments, the majority of what I will speak about is that second research bucket. And that is the product-specific research required to support a modified-risk tobacco product application, but I also will touch out to some of the others as well.

So key takeaways from our perspective -- when I speak of the industry, I'll speak, most importantly of course, of the RAI tobacco operating companies. Industry already does most of what IOM recommends. Some of the IOM recommendations -- and I'll elaborate on those in a moment -- appear to be unreasonable, unworkable, and I'll point those out, as I said.

In our view, independent third-party governance is not needed, but collaboration on certain research areas could be useful in some areas. Some types of research could resolve some problematic issues. You've already heard about some of those, and I will mention some of the same

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ones and perhaps some new ones. But a key point that we would like to bring forward is that in our view, all stakeholders need to be appropriately involved. And the tobacco company itself that is sponsoring the modified-risk tobacco product application is, in our view, a key stakeholder, and they must then be involved.

So a quick view of transforming tobacco in terms of RAI's operating companies, we're committed to transforming the U.S. tobacco industry. We have invested heavily in the potential to reduce the harm associated with cigarettes, going back more than 25 years, and that continues to this day with some examples that will become clearer perhaps in a moment. And we're committed to meeting society's expectations for how a tobacco company should operate.

Just to give you a brief view of the RAI operating companies, you know, of course, perhaps the largest company is the R.J. Reynolds Tobacco Company that manufactures cigarettes and smokeless tobacco products; the American Snuff Company, which

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we acquired nearly a decade ago that manufactures traditional America moist products and other smokeless products and the Santa Fe Natural Tobacco Company.

But we've also recently acquired or developed other operating companies. One is Niconovum that operates in the nicotine replacement therapy space. It is not CTP regulated, but it is regulated by FDA's CDER. And we've recently in the last couple of years begun developing work and products and marketing in the e-cigarette category under the R.J. Reynolds Vapor Company. And as you've also heard yesterday and today, that's certainly an emerging area of great interest to tobacco companies, to other companies, and to the consuming public.

So what's our view of tobacco regulation? Tobacco products should be regulated in a manner that's designed to achieve significant and measurable harm reduction. It should obviously enhance the information available to consumers and encourage the development of tobacco and nicotine

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products that have lower risks than existing cigarettes.

I highlight the word "encourage" because if we're not careful, the burdens imposed by a regulatory scheme or other mechanisms could, in fact, discourage that development. And I think that's a wrong way to go. They should encourage those products to market and then allow the establishment over time in post-market surveillance that the products do, in fact, deliver as the pre-market evaluation suggested that they would.

The marketing of tobacco products should be consistent with constitutional protections and enhance an adult consumer's ability to make informed choices on risks and comparative risks. And as we've heard already this morning, there are certainly lots of indications where that's perhaps not being done by government-mandated warnings and other public statements by many that do not support the informed choice on risk and relative or comparative risk. And we believe that the prohibition of tobacco products is neither

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practical nor desirable.

So when we look at the evidence domains, first of all, these are the IOM recommended evidence domains for modified-risk tobacco products. There are seven. You can read them for yourself. We'll go through those in a moment.

But what I'd like to point out is that at least under the RAI tobacco operating companies, we're already actively engaged in five of those seven domains: the preclinical, clinical, abuse potential, consumer and non-consumer perceptions, and also, modeling and synthesis.

There are other research areas that could be more problematic for direct industry sponsorship. One is epidemiology. That is not a classic strength of the tobacco industry. We have explored the notion of prospective epidemiology, but there's broad scope there. That strikes us as something, particularly as you imagine a modified-risk tobacco product that might emerge in the marketplace, you would expect there would be very low penetration early on. It would be difficult to follow that.

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So you have to have a huge study design to be able to pick that up in a prospective manner.

Our view is that that's probably more appropriately done by a consortium, perhaps via the CTP's PATH study or perhaps a multi-stakeholder effort to set up a prospective epidemiology that can pick up that movement as we go forward in time. That should not be done and cannot be done efficiently, in our view, by individual companies doing their own work, looking for the penetration of a single product here or a single product there.

We've also heard some today and yesterday about populations at high risk, non-adult consumers, non-traditional consumers in general, but certainly non-adults. That is an area that we're aware that FDA had indicated a need for information there. We have tried to seek clarity from the agency on what that should look like. We have developed tools, in fact, that could be used in non-adult consumers, but we have made it clear with the agency that we will not do that research until we get clear direction from FDA that we must

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do that research and we agree on a protocol.

So you've heard that in various shades over the last two days. That is an area that could be problematic for direct industry sponsorship.

The second area of the IOM recommendations that I'd like to look at is their recommendations on study governance. So I've briefly highlighted that here in three areas: the independent oversight and conduct, the proper conduct of research, and the public disclosure of research. And you've seen these in one form or another several times over the last few days.

There's been good discussion certainly under the first bullet about third parties should be preapproved by FDA. Others have disagreed with that notion, and we disagree with that notion. I think if you set up the proper conduct of studies, you should not mandate who can do those studies. You establish the quality and performance criteria, and any vendor who meets those criteria should be able to be used.

The proper conduct of research, obviously,

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there are standards and principles of good research guidance, an ethical view that we clearly believe should be adhered to. And then the third recommendation that IOM suggests is that modified-risk tobacco products sponsors should be required to place all data in a public repository.

So quickly through our view of those recommendations. In our view, there is no such model of governance in any other regulated industry. The domain space of pre-market-specific product application, in our view, is one solely occupied by the FDA and the product sponsor, and that is very clearly our view.

So based on that, the industry has the right and the responsibility to develop that pre-market application for its own products, and that will include various elements of research. But more importantly, FDA has the right and the responsibility to review and approve that research.

So what does that mean? In the current day and age, since 2009, FDA has full transparency to the work that we do for products that are in scope

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for regulation under the Tobacco Control Act. The type and the scope of studies, the protocols, the raw data, algorithms used to generate the results, marketing claims, that is all clearly within their area of responsibility.

I've heard the word "transparency" a few times in my life, actually a few times here over the last couple of days. I give you my view of that transparency as we go down to public disclosure and then, particularly, the last bullet that says "any model that precludes industry as stakeholders is unworkable."

Transparency is the full transmission of light in both directions. So if you think of a barrier like a piece of glass, that's a clear and colorless piece of glass that transmits light equally in both directions. It's not a half-mirrored glass. And I think in many cases, that's what we have today. So we believe we are rightfully and responsibly stakeholders in this debate, and we will advocate to maintain that seat at the table.

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Back to public disclosure, I think there are problematic issues around that, particularly in the pre-market stage. We're not aware of any requirement for disclosing such research in any other FDA-regulated industry. It's certainly problematic if it does not protect proprietary information and the ability to innovate, and, again, must work both ways.

So what's our approach to governance? The independent oversight and conduct bullet of IOM's recommendation. All work currently undertaken by any of the RAI tobacco operating companies that might support a modified-risk tobacco product application is already done in conjunction with third-party research organizations, whether it's preclinical chemistry, or in vitro toxicology, or in vivo toxicology, or clinical trials, or consumer perception of claims, we already work with third-party research organizations.

Those in many cases, and I would even say most cases, are also firms that work on pre-market approval processes with FDA in other regulated

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industries. So we're using the same partners that FDA is used to working with.

In proper conduct of research, all of our work is conducted by qualified researchers and is governed by everything that you would expect it to be governed by: written protocols, contracts that specify data retention policies, statistical analysis plans mentioned earlier and ethical review where appropriate for human work.

What does that mean? That means that the laboratories we use are either accredited. Many of them operate according to GLP, and certainly all of our human clinical trials are conducted in accordance with GCP. FDA has full visibility to any and all of that for currently regulated products that it desires. They have much of that data through a variety of processes already, so there is full transparency there that they already have and can exercise and will exercise into the future.

So just in summary, some issues with third-party governance, there's no precedent model

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in any other FDA-regulated industry. There's certainly the potential for the industry and the FDA rights and responsibilities to be relinquished if governance is sort of contracted out to a third party. And in our view, it certainly maintains and furthers the tobacco critics' desire to denormalize the industry rather than treat the tobacco industry as a legitimate stakeholder.

But there are some opportunities as well. We realize that. Certainly, you could improve the quality of modified-risk tobacco product-related research by opening access to more academicians, perhaps more CROs, journals for publication of research than is currently the norm today.

You could improve the transparency for all MRTP-related research, no matter which way it's coming from, no matter which side of that glass it starts on, both conducted by industry and also conducted by non-industry. And you could ensure that all stakeholders have an appropriate forum for dialogue and for engagement to share their views and work out the difficulties and the issues in

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front of them.

So in conclusion, industry already does most of what IOM recommends. Some of those IOM recommendations appear to be unreasonable and unworkable in some cases, and the independent third-party governance not needed, but collaboration could benefit some areas, again, as long as all stakeholders are appropriately involved.

Thank you.

(Applause.)

MS. DILLEY: Time for one or two questions.

MR. MYERS: Matt Myers with the Campaign for Tobacco-Free Kids.

In talking about the transformation of the industry and its approach, do you think it's appropriate for FDA to consider the broad public health issues that are raised?

DR. OGDEN: The broad public health?

MR. MYERS: The public health standard.

DR. OGDEN: Oh, absolutely. Yes.

MR. MYERS: Then why is your company

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actually suing the FDA, saying that it goes beyond what they should be allowed to do?

DR. OGDEN: Just like myself, I'm a private citizen. Our company is a corporate citizen. And any agency or any corporate entity has the right to make sure that their rights are protected, to make sure the law is being followed appropriately and not overstepped.

MR. MYERS: So how is FDA supposed to deal with you in a transformative situation where the organization you're representing says it's illegal, from your point of view, for them to even consider the broad public health measures that are at the heart of this dialogue?

DR. OGDEN: I'm not sure what you mean by the broad public health --

MR. MYERS: The public health standard that underlies the very discussion that we're having. I'm just trying to understand how that dialogue takes place when in one breath you're saying we're transformative, we're concerned about these public health measures, and in another breath, the

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institution you represent says to the FDA the very consideration of the public health considerations, this public health standard, violates our legal rights. I'm just trying to figure out how that dialogue --

DR. OGDEN: Well, I'm not familiar with the exact case of which you speak, even if there is such a thing, so I couldn't address that.

MR. MYERS: Well, in Kentucky, you sued, and among the many things you challenged was not only a bunch of First Amendment issues, but the very legal standard -- the consideration of the public health standard is one of the core issues raised by your company.

So I'm just trying to figure out how that dialogue takes place and whether you --

DR. OGDEN: I'm not a lawyer. You are. I'm a chemist. But it strikes me as reasonable, as everyone has acknowledged, the public health standard is something new. It's new for FDA. It's new for us. It doesn't strike me as unreasonable as a chemist to ask the question is that a fair

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standard, and perhaps it is. That's fine. But it's worth, I think, asking the question to make sure that it is what is intended by the Act. It does reflect Congress' intent, and it is consistent with the laws of the land.

MS. DILLEY: All right. One more question, and then we need to move to the next presenter.

DR. BACKINGER: Cathy Beckinger, CTP.

Mike, you said I think on the summary slide, improved transparency for all MRTP-related research, including that conducted by non-industry parties. Just a clarification, could you maybe -- I'm not sure exactly what you meant there. Transparency for whom? Because you did mention that, obviously, it's transparent to FDA. So I wasn't sure who you meant transparency for as well as plans for transparency on the research that RAI is conducting.

DR. OGDEN: That's a good question. I think I can easily clarify that. I think in the pre-market world, as I've said, I think that domain belongs to the sponsoring company and the FDA. In

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the post-market world, that's different. The product would be on the market with an initially cleared or approved claim, and I think at that point, you would draw a lot of research interest. We've seen that with products we've introduced. People pick them up at the market. They follow. They do Internet-based surveys, et cetera.

So what I'm imagining there is in a post-market surveillance world where the sponsoring company has requirements for post-market surveillance, you would see post-market surveillance emerge from other stakeholders, perhaps academicians, perhaps our competition. And those types of studies would get published.

So my point there is if those data are to be considered by FDA as to whether to continue the support or clearance of a modified-risk claim, then all of that data should be in the same full transparency mode as the industry data.

So in other words, they shouldn't rely on posters at a meeting or even peer-reviewed publications. If we're going to look at the

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effects from multiple studies coming from multiple stakeholders, FDA should have the ability to see all of that data at the same level of detail.

MS. DILLEY: And you were specific to post-surveillance data?

DR. OGDEN: And it's clear in post-market surveillance. There may be some applications in other areas, but that one is the most obvious.

MS. DILLEY: And you'll be returning, Mike, for the panel Q&A session.

DR. OGDEN: Sure.

MS. DILLEY: So next is Justine Williamson who's the head of biosciences at British American Tobacco.

Presentation – Justine Williamson

DR. WILLIAMSON: Good morning, everyone. I'd like to thank the CTP for giving us the opportunity to take part in this very interesting workshop. I think none of us are going to be left in any doubt that the tobacco industry history as laid out in the IOM report has had considerable influence on the recommendations that they have put

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in place. And as a tobacco industry scientist today, I must say that history makes uncomfortable reading. It has left us with a difficult legacy and a more challenging working environment.

I think sort of two main drivers that really stick out are there is a total distrust, obviously, of tobacco-sponsored research; and, secondly, that there is a belief that the tobacco industry lacks the expertise, the infrastructure, the credibility to put together a credible and legal MRTP application.

So what I'd like to do today is speak to those two drivers from a BAT point of view, highlighting some of our experiences over the last five to 10 years, and I'll cover these areas.

Talking about BAT scientists today -- and I'll use my own department as an example. So it's a biosciences department. There are about 60 of us in the department, and we're responsible for the majority of British American Tobacco's biological testing. So that's from in vitro tox testing, through to smoking topography, through to clinical

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studies.
Now, two things to note about these guys is their average age is 37 and a half, and the average length of service at BAT is eight and a half years. And these guys, pretty much all, bar one or two, including myself, joined British American Tobacco post-2000, at a time when the company was acknowledging the health risks associated with smoking, and had on its corporate website that smoking was the cause of serious and fatal diseases, lung cancer, COPD and heart disease. Also, these guys joined an R&D that had, and still has, very active reduced tox programs and harm reduction programs.
So in terms of the expertise that we have -- and now we'll talk about my own guys and in the wide R&D. I've split this into three areas, and I'll start by talking about the historical expertise we have.
So we've had an R&D in Southampton for over 50 years, so we actually have decades of experience in some areas: combustion science, smoking

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topography, toxicology. And some very good fundamental research has come out of that time. I think probably many of you in this room are familiar with the work of the late Richard Baker whose seminal work on combustion science, twice published in Nature, really helped at that time in understanding the fundamentals of the complexity of smoke.
Then obviously with the publication in 2001 of the IOM's Clearing the Smoke, this brought on a new era in tobacco science because it was then we knew it wasn't -- it's not enough just to reduce toxicants in products. What that told us to do is it told us to show -- we need to show how that links to reduced exposure and then how that in turn links to actual reduced disease risk.
So this was a complex and daunting challenge probably for all of us and led to a huge expansion and diversification of our research programs. We didn't have the expertise in house to do that, so we had to recruit from the pharma, medical, government, academic backgrounds to be able to get

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that expertise to start looking at biomarkers, in vitro models of disease, clinical studies.
Now, at the same time, as a company, we were looking at how we develop products along the risk continuum, and we bought a smokeless tobacco company, a Swedish one, and we moved into snus. So this was a time for us also then, as we're moving into this area, to become familiar with smokeless tobacco science.
So now, more recently, we understand it's obviously not just enough to understand what the reduced-risk products potentially can do for a consumer in terms of individual disease risk, we also now need to understand what that's going to do to consumer behavior and population effects, population health as a whole.
So all of us -- and we've heard today -- are sort of moving into these new areas. We're all sort of finding our way a little bit. And so risk perception, market surveillance, I should have on here abuse liability, are all areas we're starting to come to terms with and work out what we should

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be doing around these.
Most of you know as well that British American Tobacco, we have a wholly-owned subsidiary company, Nicoventures, a nicotine company. We've recently bought an e-cigarette company, CN Creative, and we are developing e-cigarettes in house as well. So e-cigarette science, again, is an area of expertise that we are coming up to speed on, really, as fast as we can.
We've been using the word "transparency" a lot, and it's good, so I'm using it on my next four slides. So I think that it's viewed by some and it was highlighted in the IOM's report that the industry is profoundly isolated from the mainstream scientific community. And one of the examples that is given is that many journals will not accept or publish tobacco-funded research.
Now, of the 24,000 or so journals that are out there, approximately a third are science, technical/medical journals, and to our calculations, we think there are roughly around 9 or 10 that have explicit bans on publishing

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tobacco-sponsored research. Thankfully, from our experience, the vast majority of journals judge a manuscript on its scientific merit and not on the funding source.

So with that said, we've over the past five years published about 100 papers in over 45 journals. And the areas we're publishing on are very much associated with some of the questions that the CTP are asking, their 56 priority questions, and very much are hopefully going to help add to the tobacco science, regulatory science field as a whole.

We have at least 20 of our top scientists, regular referees for over 40 journals. And, ironically, one of the journals that won't accept our publications will accept our free expert labor to review manuscripts.

(Laughter.)

DR. WILLIAMSON: Conferences, we go to numerous conferences. We go to tobacco industry, tobacco control, public health, and niche scientific conferences like analytical chemistry,

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toxicology, those sort of areas.

Why do we go to conferences? The same reason as any other researcher goes to conferences, is to inform our research. It's to ensure we're at the cutting edge of research. It's for the continuous professional development of our scientists. And it's also to ensure that our science is out there and is up for scrutiny from the external scientific community.

On the flip side, we feel we have expertise, knowledge, data that others are interested, especially as this tobacco regulatory science field is growing. And just last week, we were at the SOT and SRNT with seven posters on priority toxicants, clinical studies, in vitro models of exposure, so all things that are of relevance to some of the things we've been talking about today.

Very quickly, we've had our dedicated BAT science website for about five years, giving an overview of our harm reduction research programs. All of our publications are referenced on there, and where possible, we try to go for open access

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journals very much now so people can get hold of those posters on there. And year and year, we're seeing an increase in interest in the site. Last year, we had 82,000 visitors and 282,000 hits.

Finally on transparency, we have a visitors welcome policy at our R&D center in Southampton. And we're not just having our own company, BAT staff, come down to understand more about tobacco science and the research we're doing. Of the 34 groups that came to us last year, two-thirds of them were external visitors. So that included external scientists, included publishers, regulators, politicians, journalists, analysts, a whole broad range of people coming through.

The popularity for people to come down and learn about what the tobacco industry is doing in research has meant we've now developed interactive science exhibition and lab tools, all of which are staffed and led by our practicing scientists.

Over the years, we've hosted a number of external meetings. And we've recently had completed a 300-seat auditorium, so we've been able

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to host larger conferences. We hosted the British Carbon Group conference last year, and in May, we'll be hosting the In Vitro Testing Industrial Platform meeting.

So I think what we've found when it comes to research partners is that our sort of decades' long effort to be as open and transparent as we can be has helped when research partners are considering whether they would like to work or collaborate with us. So in terms of -- and what we're finding is that being transparent around our harm reduction approach and our commitment to developing and assessing reduced risk products has meant that high quality CROs are willing to work with us and co-publish with us.

Academic research organizations, yes, this is more of a sticky one. And the bans in certain universities in the U.K. and the U.S. do mean we have not been able to work with some research groups we would perhaps like to. But we know that the global scientific community grows ever stronger. And though we would like to be funding

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research in our own background, we can go to expertise literally around the world now. And over the past five, six years, we've had at least 15 academic research collaborations going.

There's some question about the credibility of research organizations, academic organizations that take funding. And we've co-published with Cornell, with the Max Planck Institute in Germany, and with Cambridge University in the U.K. So I think they would consider themselves to be credible.

Commercial partners, yes, we do a little work with commercial partners. My own group right now, I'm working to help characterize a primary human lung cell type to work out the metabolic competency of that. We'll co-publish with those partners. We're also organizing a ring trial of an in vitro health smoke exposure commercially available system with a number of partners, including the supplier.

We've been a strong member of CORESTA for many years and do believe that -- this is the

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scientific industry group, and we do believe it's a strong forum for developing good analytical, good technical methods that, again, will be of interest to the tobacco regulatory science field.

We've been invited into multi-sector expert groups, and this is because the breadth of our research is growing. So that's with pharma, cosmetic, industrial-type partners.

We see the TCORS and the NIH funding opportunities as an excellent way to add to the research base that's going to drive tobacco regulation. And what we would say is that any people interested in sharing any of our expertise or analytical services, or products, we're happy to discuss those types of partnerships.

So moving onto governance and similarly to what the first two speakers have said, our research governance includes registration of clinical trials. So it includes oversight of our clinical studies with ethics committees. We only work with CROs to the highest GxP standards, and we have been moving to increase our own internal standards to be

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able to get up to high regulatory standards. And we have just had -- we're going through a huge overhaul of our quality management and IT systems, recruiting guys from pharma to help us do this in order to meet those standards.

Others have touched on disclosure of data. Yes, we agree. We would similarly support the principal of disclosing data, have been discussing that pretty much since we had our website. So again, happy to discuss that.

So similarly to the other guys, with the correct governance that the FDA have used for pharma industry, with all this correct governance in place, we don't actually necessarily see the need for independent, third-party research for the majority of research. However, as agreed by the other guys in the industry, consideration for specific areas like vulnerable groups, research on adolescents, then, yes, we should look at that.

So to summarize then, we are a new generation of tobacco -- and I should say tobacco and nicotine, now, industry scientists, and we are

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determined to leave a more positive legacy than our predecessors. We believe we have significant expertise growing in other areas, and because of our sort of transparent approach, we believe we can engage with enough experts to be able to, in time, produce the credible data that the FDA would like to see.

Our views are very much in alignment and agreement with the vast majority of the IOM's views, and, as I said, with correct governance in place. So independent third-party research is probably only required for those sort of certain areas that have already been discussed.

So I think that's just about me. And I think probably just to finish, I would agree that we are moving into a new era. And it's my personal opinion that this new era with new regulatory environment, new products, new people mean that all the ingredients are in place now for us to really make a positive impact on tobacco science and public health.

Thank you.

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(Applause.)
MS. DILLEY: Quick one or two questions.
David.
DR. ASHLEY: Thanks. I was very interested in the diagram you had on your second or third slide about kind of the changes of research and how there was traditional research, and you've been adding -- you've been moving into new areas.
In relation to that, are you-all continuing to do developmental research on smoke products, or have you pretty much moved beyond that and are really looking at new products and new directions?
DR. WILLIAMSON: Yes, we have programs in all areas. So we are looking to reduce the toxicants within our combustible products, as well as looking at developing reduced risk -- well, hopefully reduced risk -- smokeless tobacco products and nicotine and e-cigarettes, so across the board.
MS. DILLEY: One other question? Anyone?
(No response.)
MS. DILLEY: Thanks, Justine. We'll have

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you come back up when the full panel and respond to Q&A.
So our next speaker is Jeffrey Walker who's with Altria Client Services.
Presentation – Jeffrey Walker
DR. WALKER: Good morning. My name is Jeff Walker. I'm the vice president and the chief medical officer at Altria Client Services, speaking today on behalf of Philip Morris U.S.A. and U.S. Smokeless Tobacco Company. I want to thank the agency for the opportunity to speak today in reference to third-party governance of industry sponsored research.
In 2011, the IOM published its report on the scientific standards for the evaluation of MRTPs. In this report, as we know, the IOM recommended the establishment of a third-party tobacco research governance entity for studies to evaluate MRTPs. The report states that the role of governance is to ensure the proper conduct of research. Recommendation 10 from the IOM states, and I'll quote this, "MRTP sponsors should consider use of

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independent third parties to undertake one or more key functions, including the design and conduct of research, the oversight of specific studies, and the distribution of sponsored funds for research. Such independent third parties should be approved by the FDA in advance of the research." And that's the end of the quote.
The IOM report also describes several governance models, although it acknowledged that those models have not been traditionally used in product-specific applications.
The IOM report raised several considerations, and we've heard a lot about those over the last couple days for industry-sponsored tobacco research. To Justine's point, transparency; independence of researchers from industry influence; use of established research methodologies and principles; ethical study conduct, including human subject protections; and mechanisms to ensure data accuracy and data integrity.
The common underlying theme is ensuring that

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the industry-sponsored research results in accurate, unbiased, and scientifically relevant data that enables FDA to make informed regulatory judgments.
The regulatory framework established by the FSPTCA, the Family Smoking Prevention and Tobacco Control Act, provides the necessary elements of governance to ensure that industry-sponsored research meets the expectations and requirements of the agency as it implements its regulatory authority.
As such, third-party governance is duplicative and unnecessary in light of the agency's regulatory authority. This does not mean we oppose the use of third parties. Rather, it's the proposed governance by third parties that we consider problematic. As I will discuss, third parties are currently serving important roles and will continue to do so.
I would like to address first how FDA can apply its authority, its knowledge, and its processes to provide the governance of tobacco

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industry-sponsored research. Under the FSPTCA, Congress granted FDA broad authority and broad enforcement authority over manufacturing and marketing of new and modified-risk tobacco products, including pre-market authorization authority. FDA can also provide direction, oversight, and guidance to sponsors for the conduct of tobacco research.

With regard to transparency, the FSPTCA created a regulatory framework that requires industry openness and interaction with the FDA. Since June of 2009, the agency has access to manufacturing facilities, product formulas, and information relating to the production and other aspects of regulated tobacco products. The agency has authority for and has conducted unannounced site visits to manufacturing facilities. The agency has also conducted site visits of tobacco product research and manufacturing facilities to learn more about the industry.

In addition, the FDA has authority under Section 904 of the FSPTCA to access an extensive

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and unfiltered array of industry documents pertaining to the health, toxicological, behavioral, or physiologic effects of current or future tobacco products.

From my 19 years of working in industry, 17 years of which I spent working in medical devices, pharmaceutical development and combination products, I've observed industry-sponsored research under FDA regulation is a transparent process. It typically includes sponsor meetings with the agency prior to, during, and following the conduct of a wide range of scientific studies, both preclinical and clinical. The FDA also obtains from sponsors original data, reports and internal findings related to the research and development of new regulated products in pre-market applications.

In short, FDA implements regulatory processes that assures sponsor provides the agency with data in its unaltered and original form. Under the Act, FDA has an even greater degree of transparency with tobacco-sponsored research than it does with pharmaceutical or medical device.

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With regard to scientific standards for the breadth and conduct of industry-sponsored research, the IOM report stated that the industry lacks the ability to produce comprehensive and credible data about tobacco products. This perspective fails to consider the agency's role and their ability to establish and apply scientific standards to tobacco industry-sponsored research in support of product applications.

The FDA has tremendous expertise in regulating a wide variety of companies across the food, drug, dietary supplement, biologic and medical device fields. Many of these companies routinely conduct sponsored research in support of product applications, and the vast majority of these companies conduct high quality, industry-sponsored research that complies with acknowledged standards of preclinical and clinical practice and ethical study conduct through the use of GLP and ICH GCP guidelines. FDA can and I suspect will establish similar standards for the conduct of tobacco industry-sponsored research.

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With regard to independent study conduct, other regulated industries use third-party independent, internationally-recognized CROs, contract research organizations, to obtain high quality data that is used by the sponsor in support and by the FDA in the evaluation of pre-market product applications.

In most stages of research, the CRO is responsible for the selection of high qualified investigators, implementation of study protocols, data monitoring, and quality audits. The CRO can also establish independent data safety monitoring boards, data monitoring committees, and other functions that are independent of sponsor interference.

In our view, the FDA can apply the knowledge gained from overseeing other industry research and its authority under FSPTCA to enable similar approaches for industry-sponsored tobacco product research.

With respect to industry engagement, FDA draft guidances on new and modified-risk product

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applications encourage the sponsors to solicit feedback from FDA on planned studies in support of product applications, including feedback on study design, statistical analysis, data collection, human subject protections.

The agency has also issued guidance on how industry and investigators can request and conduct such meetings with the agency. These meetings are critical opportunities in the regulatory process, both for the agency to provide research guidance and for sponsors who seek to gain agency feedback on planned studies to support product applications. Effective engagements with FDA on study design and study conduct will enable sponsors to provide FDA the requisite and scientifically relevant data that it needs to evaluate product applications.

I'd like to turn to the potential role of third parties in industry-sponsored research. First, such interaction is contemplated by the regulatory framework. FDA can and does solicit third-party expertise and input as it implements its regulatory authority. For example, the FSPTCA

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established a TPSAC, Tobacco Products Scientific Advisory Committee, to provide FDA with advice, information, and recommendations regarding modified-risk applications and other regulatory matters.

The agency has solicited third-party expertise from the IOM on the topic of standards for modified-risk products. Further, the agency has the authority and the financial resources to solicit input from highly credible and independent sources of scientific expertise that it believes beneficial in the conduct of its duties, including those related to industry-sponsored research.

Moving forward, both FDA and sponsors could use third parties to develop methods, conduct studies, or analyze data for new or potential modified-risk tobacco products. These third parties may include qualified contract research organizations, independent scientific experts, or academic institutions.

Third parties may be particularly beneficial in research related to the impact of tobacco

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products in certain populations such as nonusers, former tobacco users, or youth, or in the area of abuse liability.

Overall, while we don't endorse a single model or approach, we believe that there are several principles that should govern the use of third parties by FDA and by sponsors. First, FDA retains its industry governance and oversight authority. FDA should not abdicate or share this authority.

Sponsors should retain the responsibility recognized by the FSPTCA to generate and submit to FDA the science and the evidence required for pre-market applications. And sponsors should retain intellectual property rights and protections associated with study results or data analysis as accomplished in other FDA-regulated industries.

So in closing, third-party governance of tobacco industry-sponsored research is duplicative and could add unnecessary complexity to FDA's regulation of tobacco products. The agency has the expertise and the authority to advance tobacco

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product regulation in a science- and evidence-based manner without abdicating its governance authority to a third party.

However, third parties can serve several important functions. FDA should seek input and expertise from a variety of third parties that can contribute to implementation of its congressionally-mandated authority. Further, the FDA and sponsors could use third parties in a principled way to develop methods, conduct studies, or analyze data related to new or potential modified-risk tobacco products.

How the agency implements its authority over tobacco products, including its oversight of industry research, is still unfolding. We expect to engage and work constructively with the agency to generate the requisite scientific evidence to support new or modified-risk tobacco products.

Thank you.

(Applause.)

MS. DILLEY: A couple of questions?

(No response.)

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DR. WALKER: Thank you.
MS. DILLEY: Very straightforward. Thank you.
Michael Hufford is our last speaker. He's the chief medical officer, e-Nicotine Technology.
Presentation – Michael Hufford
DR. HUFFORD: Thanks so much for your time and attention today. By way of disclosures, I'm co-founder and chief medical officer of e-Nicotine Technology, a small healthcare company devoted to harm reduction and helping smokers transition off of combustible tobacco products to safer, clean nicotine products. I also want to note that neither myself nor any of my colleagues at e-Nicotine Technology have ever been employed by nor taken money from the tobacco industry.
I'm going to be touching on a number of points today, both the IOM report. I also am going to touch on both the promise and some of the perils of using the pharmaceutical drug development as a role model for the development of modified-risk tobacco products, and end by sharing some thoughts

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on the critical role, I think, that innovation can play at an intersection of science and regulation to help potentially dramatically transform the tobacco control landscape.
My perspectives on these issues are shaped by my experience. I started off as a nicotine researcher doing research in cue reactivity and using ecological momentary assessment to try to better understand the relapse process amongst smokers trying to quit. I became disheartened with my own research insofar as if you track the number of peer-reviewed publications over time but plotted against the average abstinence rate, thanks to smoking cessation interventions, the two curves show remarkably little relationship to one another.
So I got involved in drug development, and, again, some of my perspective is shaped by that experience as well. I was fortunate to work in both fields of orphan drugs as well as large pharmaceutical markets around obesity, also helped to get a drug approved, Naprosyn, for the management of fibromyalgia through CDER. So some

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of my perspective on this is also shaped as a drug developer.
Lastly, I've also helped to grow a number of specialty contract research organizations focused both on electronic patient-reported outcomes and neuropsychological assessment in clinical trials. So I also wanted to speak from that perspective from the trenches much as Donald Graff and Eric Donny have done before me.
So in terms of the IOM report, e-Nicotine Technology supports each of the 12 recommendations contained in the guidance document. And, indeed, I thought it was interesting that that document also foreshadowed companies like e-Nicotine Technology; we are by no means the only one.
Getting into this space, we absolutely should face the same high rigorous standards for scientific conduct and transparency in all of our research; although I think it's also the case that coming at this, whether you're a pharmaceutical company, a biotech company, or a company explicitly focused on the development of novel products in

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this space, we may not have to overcome the same hurdles in maintaining or restoring credibility to their research as is noted in the report.
I also wanted to note the electronic nicotine delivery devices I believe should receive an appropriately abbreviated and expedited review if they're shown to deliver far fewer harmful or potentially harmful constituents as compared to conventional cigarettes.
Indeed, the Light Touch regulation, that in Britain the medicines and healthcare products regulatory agency or MHRA is currently considering, I think may be very appropriate to this industry and, in fact, in the best interests of public health. That Light Touch regulation, in my mind, should address a number of critical issues that aren't being governed today; so PK data, for instance, to know that you're getting a consistent dose of nicotine, which is shown to be deficient in many current products.
Evidence of quality manufacturing and batch-to-batch reliability. This is known in the

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pharmaceutical industry as CM&C issues, chemistry, manufacturing and controls. There is no excuse for contaminations like diethylene glycol in a consumer's use of a product that should contain only nicotine and propylene glycol. And, in fact, wearing my drug development hat, that's a fairly easy problem to solve. That's a very tractable problem.

So PK data, evidence of quality manufacturing, screening of marketing materials to be used in marketing these products, and post-marketing surveillance, I think would represent a very reasonable regulatory middle ground, enabling innovation to come forward with less harmful products and not stifling the sorts of innovation, which I'm going to talk about in a bit, that I think historically has led to radical transformations in other industries. And I think we're on the precipice of doing just that in this industry as well.

I want to talk just a little bit about the pharmaceutical drug development and using contract

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research organizations for some of this research. Again, Donald Graff just did a wonderful job articulating a number of the strengths of the model. I won't belabor that. This is just a plot of the global location of CROs by continent and country. There's tremendous bandwidth here to get this research done. Indeed, this is a $24 billion industry in 2010, so there's tremendous bandwidth and expertise if we can find an agreeable way to use that expertise to help MRTPs move forward.

I in no way envy the CTP's path in front of them insofar as almost any action they take may well be litigated by big tobacco as well as be the subject of considerable public controversy. That's also the case with some very prominent acts that govern CDER and the development of drugs and medical devices.

So the Prescription Drug User Fee Act, known as PDUFA, was implemented in 1992 to help speed the review of applications for new drugs to the agency. It has succeeded in doing that. I think the facts largely bear that out. But it's also certainly the

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case that you can find both in the peer reviewed literature and certainly in the blogosphere folks criticizing that act, believing that it creates too cozy a relationship between the pharmaceutical industry and the FDA, or that too many of the funds are used for things other than safety, for instance.

I raise all that only to note that at the end, as Voltaire said, "The best should not be the enemy of the good." Almost any action the CTP takes is bound to develop some controversy. Public opinion will land in a variety of -- along a spectrum for almost any actions that you take. Now, three years in to the passage of the Family Smoking Prevention and Tobacco Control Act, I do hope that we can move forward swiftly.

I did want to just note one caveat about the perils of the CRO model, though. Many of you may be familiar with Moore's Law. This was a prediction back in the mid-60s, believe it or not, that over the history of computing, that the number of transistors on an integrated circuit would

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double approximately every 24 months. In fact, that has exactly been the case. This is a field that has just innovated time and time again and shown just dramatic and radical innovation. It is testimony to what Alan Kay said, that "the best way to predict the future is indeed to create it."

Sadly, when it comes to drug development, the model is almost on its head. This is from a Nature publication by Scannell, et al. They take about Eroom's Law. Eroom's Law is the number of new drugs approved by the FDA per billion of U.S. dollars, inflation adjusted, spent on R&D has halved roughly every nine years. So, unfortunately, when it comes to drug development, the curve goes in the opposite direction. We spend more and more money and take more and more time to get each drug approved.

Now, there's a lot of reasons for that I think are shared across the regulatory environment, the scientific environment, as well as the CRO environment. So as we think about relying on CROs for some of that work, we need to be aware this is

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a crowded space. This also tends to be fairly low margin work in CROs. And so you also have to think about the economic incentives to get companies to choose to do MRTP research versus other pharmaceutical types of research. It's also the case that the costs associated with developing drugs is increasing astronomically.

I wanted to start to transition, though, to the role of innovation then and how it intersects with the regulatory landscape, and, in particular, this issue of third-party governance and how we can best help modified-risk tobacco products that can potentially meaningfully impact public health move forward as quickly as possible.

This is from an article by Bernard Munos, Lessons from 60 Years of Pharmaceutical Innovation, showing that, in fact, large companies are increasing responsible for fewer and fewer products. Small companies are responsible for those. I'm going to draw a parallel to big tobacco in just a moment. And another publication also looked at the importance of new companies in drug

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discovery and looked at a decade of new products and found, in fact, a majority were coming from biotech companies or university discovered and then transferred to biotech companies. They tend not to come from large industry.

With that, I'd like to transition and talk a little bit about the role of innovation and its intersection with science and regulation in this field.

Almost this entire book is quotable, The Structure of Scientific Revolutions from Thomas Kuhn, but I thought this quote was in particular very apropos to the current environment. It says, "As in manufacture, so in science, retooling is an extravagance to be reserved for the occasion that demands it." And I would offer to you that this is absolutely an occasion that demands it.

In fact, in terms of the retooling, one of the things if you haven't read, I would urge you to take a look at some of the work that Clayton Christensen has published on the Innovator's Dilemma, as well as on healthcare, the Innovator's

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Prescription. It's very relevant reading because it talks about how large entrenched industries that at one point in history seemed just so impenetrable and formidable can be destroyed by radical innovation that eats away at them from the margins. And, indeed, Clayton Christensen talks about the role of innovation first in industries drives centralization of knowledge and skills. Innovation plays oftentimes a key role in building big business. But then just as predictably, given the right regulatory environment, the right science, and I'm going to argue the right innovation, innovation then plays a reciprocal role in decentralization.

So we're going to talk a little bit about what that innovation is likely to look like and how regulation can help be sure not to impede that innovation.

So we're going to talk about there's also an important difference here between radical innovations and incremental innovations. Incremental innovations tend to come out of large

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companies. That's true whether it's the pharmaceutical industry, whether it's the tobacco industry. Radical innovations very often are driven by smaller companies pursuing radical ideas. So who's it new to? Well, radical innovation is new to the world. Incremental innovations are new to the company. The risk profile of radical innovations tend to be high relative to incremental innovations, and there are some unique challenges both in terms of requiring new competencies for radical innovations, destroying existing organizational competencies oftentimes, and oftentimes having to get involved in social and systematic change to bring those innovations about. By contrast, incremental innovations tend to utilize existing skills present in large companies and perpetuate existing social practices.

Relationship to the status quo. Radical innovations tend to challenge the status quo. Incremental innovations tend not to. But at the end of the day, I think what we need from a public health perspective to help people transition off of

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these incredibly harmful and, in fact, deadly combustible tobacco products is really a step change in performance versus a gradual performance improvement.

So I'd like to walk you through what I see as a certain formula here. As Brandt articulated just wonderfully in the Cigarette Century, the cigarette industry, the modern tobacco industry, had a number of dramatic innovations. And I should note that innovation is fundamentally amoral, not that it's immoral but it's amoral. It's really outside the scope of right or wrong. Innovation can accomplish great things, but whether those are good or bad really depends on what direction you point the innovation towards.

In this case, in the late 1800s, say, you had it pointed toward profit alone. And so the flue-curing of the leaf to change the pH so that the smoke could be taken into the deep lung, which radically accelerated the absorption of nicotine and its activation of the nicotinic alpha-4 beta-2 receptors in the brain and dopamine release, that

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was a radical innovation at the time. The Bonsack machine acquired by the Duke family back in 1881, a radical innovation.

There have been countless thousands of incremental innovations, including the use of ammonia, for instance, to enhance the addictive profile of some cigarettes.

So this is what you have. You have a field that had a lot of innovation. And when you combine that with a lack of scientific insight -- that's not a completely accurate descriptor. I think, in fact, as has been well chronicled -- and this particular page is kind of hard to read, but this is from the famous Doubt is Our Product memo. There was a combination of a lack of understanding of causation and lung cancer, in particular, as well as an active obfuscation of some of that data coming out of industry.

But if you combine that innovation, then, with a lack of scientific insight, combined with a lack of regulatory oversight, well, we fundamentally have the problem that we have in

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front of us today. This is an image that I took from the World Lung Foundation's Tobacco Atlas. Each pack of cigarettes on this particular slide represents 30 billion cigarettes. I will not attempt to address the epidemiologic disaster that this represents.

Sir Richard Peto, for those of us who were at the Society for Research on Nicotine and Tobacco last week, did a fantastic job reviewing the epidemiology and the estimated public health impact of this industry in the 21st century, claiming potentially 1 billion lives if something is not done.

I don't want to belabor that point. What I want to focus on is this other plot from the Tobacco Atlas because I think it plays a key role in how innovation can be leveraged to bring about a dramatic change to this industry. In case you can't read it, this notes that "Tobacco company profits in 2010, the combined profits of the six leading tobacco companies was $35 billion." That's profits. That was equal to the combined profits of

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Coca Cola, Microsoft, and McDonalds in 2010.

Why do I focus on these revenues? This isn't to shame anyone about having a big business. This is because, as Mary Lasker, the noted cancer advocate and philanthropist noted, that "money is frozen energy and that it unfreezes itself when you pay people to work." And the point I want to drive home to you is that is a tremendous amount of frozen energy. That is a market that under the right regulatory framework, I think venture capitalists could potentially flock to.

Venture capitalists in this country -- venture-based companies provide 11 percent of the private sector jobs in this country. The venture-backed companies are responsible for about 21 percent of the U.S. GDP, invest about $30 billion in these companies.

I don't know how many of you saw this recently in the news. James Cameron and some Google executives made a venture-backed investment in asteroid mining. Do whatever you want with your money, I suppose.

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What strikes me about the tobacco industry is in the U.S. alone, it's an $80 billion industry, responsible for 440,000 deaths per year. This is a potential venture investment that has the rare opportunity to both do good but also do very well. I think it's possible both to save lives and to potentially generate a huge return on investment in innovation in this sector.

So now I want to rewrite that formula for you about innovation now pointed in a different direction. These are a variety of different products in a variety of different stages of development. I'd like to note a great quote I came across from Michelangelo. He said, "The greatest danger for most of us is not that our aim is too high and we miss it, but rather that our aim is too low and we reach it." So certainly, a number of innovators in this space, including e-Nicotine Technology, intend not to fail by the latter part of that clause, but if anything perhaps, by the former.

So for ourselves, our focus on innovation,

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our products shown here on the left, combines deep-lung deposition of pure nicotine and propylene glycol in a 1 to 3 micron particle to the deep lung to mimic the rapid pulsatile pharmacokinetics of a smoked cigarette. But onboard e-health tools, I think for the first time, enable the user to choose what relationship they want to have to nicotine, whether that's complete or partial, coming off or transitioning off of combustible tobacco products, or weaning off of nicotine entirely. Also, electronic controls enable you to have parental lockouts, enable you to do things like prevent overdose.

My point being that research can inform policy. Policy can also inform research. But at the end of the day, tobacco control is about taking action. And action fundamentally can be taken either by big tobacco with incrementally innovative products or other products that they've developed, or it can be taken up by the entrepreneur.

So if you combine this innovation, then, with the scientific insight that we have today,

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that, in fact, nicotine is not a direct carcinogen -- and this is a slide from a 2010 meeting on NRTs that the FDA hosted. The figure to the right, by the way, is hard to see here. It was actually created by an ad agency in Saudi Arabia. It lists in microscopic print all 4,000 chemicals listed in a cigarette. It's a great image if you can find it online. It shows up quite better there.

So if you combine that innovation with the scientific insight that we now have about nicotine, combined with the newly empowered regulatory oversight, what we have, I think, is still just a tremendous amount of work cut out for us. We still have an enormously large industry. It really is in every sense of the word a Goliath. I suppose like any entrepreneur, I believe, though, that I both have a sling as well as a particularly hard rock.

Lastly, I want to note, in terms of its interaction with CTP in particular, I'm not sure how many applications CTP anticipated getting. I was at a session again at SRNT last week talking

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about more than 3,000 applications have been submitted. I thought I saw that perhaps 10 of those were MRTPs. So what may have started like that, kind of started looking like this, and from there.

This is not a WikiLeaks photo, though I am suspicious that there's a room somewhere in this building that may well look a lot like this. This is sort of the potential to induce drowning via paper. I studied this figure carefully, and I think in the -- I think I saw my meeting request, which is on the bottom.

(Laughter.)

DR. HUFFORD: So one point I wanted to make, in terms of moving forward with this sort of volume of applications, though, in all seriousness, is a focus on best ideas versus most ideas, because I think fundamentally what we need here is radical innovation versus incremental innovation.

So if you imagine a variety of products that have submitted, in fact, clearly hundreds of applications, and if you think about a typical

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combustible product with numerous different blends of tobacco being used, there's some n factorial number of ways that those products can be combined. So the potential here to sort of drown in applications is likely quite real.

You could certainly review them in the order received. I would argue from a public health standpoint, it may be best to review each company's best ideas first. Have either them potentially nominate what they think their best idea is, or perhaps you take that on yourself, which has the potential for the most public health impact.

And if you did that, appreciating that each company would have to be partially or wholly-owned subsidiaries -- you don't game the system -- can submit as many of these applications as they have, but the best ideas are nominated and reviewed first, and that that system would have as a virtue -- perhaps not grinding to a halt by virtue of hundreds of incremental applications and also focus on radical innovation, which I'd argue both historically and across multiple industries comes

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from smaller companies, it would help to ensure that those things have equal access for FDA input and review.

So by way of summary, I'd like to reiterate our support for the IOM report on scientific standards for the studies on modified-risk tobacco products. I think there's a lot of potential benefit, some drawbacks, to using the pharmaceutical drug development model to get some of that research done. And as I hope has been clear, I see a key role for innovation in potentially radically transforming this industry.

I wanted to end as the IOM report began, with this note, that "Knowing is not enough. We must apply." And that "Willing is not enough. We must do."

Despite this being a very different presentation and a very different audience than a typical venture presentation that I might give on behalf of my company, I'd like to end with the exact same observation, which is I firmly believe we're working on the most important drug delivery

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problem on the planet, and I hope that you share our vision of a smokeless world.

(Applause.)

MS. DILLEY: Thank you, Michael.

A couple of questions for Michael before we have the other panel members come up and start our full Q&A session. So question over here.

MR. MOYNIHAN: Yes, just a very simple clarifying question. You alluded to a meeting request, so would you mind saying when you submitted it?

MS. DILLEY: Could you introduce yourself, by the way, just so we can --

MR. MOYNIHAN: Michael Moynihan, Goodrich Tobacco.

MS. DILLEY: Thank you.

DR. HUFFORD: I actually submitted it on my birthday, December 5th, so it was a gift to myself.

MS. DILLEY: Any other question for Michael? Matt?

MR. MYERS: Matt Myers, Campaign for Tobacco-Free Kids. Thanks, that was fascinating.

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So you talked a lot about the product innovation. I'm curious, because the second component of what you said in terms -- spoke in terms of your goals was -- if I'm interpreting it right and if I'm wrong, tell me -- moving people from products that kill people to products that you believe don't kill people.

DR. HUFFORD: That's correct.

MR. MYERS: Which is at the core of the public health standard. So how would you envision doing that as well under your model?

MS. DILLEY: You mean doing that --

MR. MYERS: It's the moving piece because MRTP -- the Section 911 looks at the product, but it also looks at what's the population effect of the product. And, therefore, you have to have a plan for the population effect to understand that.

DR. HUFFORD: That's a great question. And I was sharing with a colleague just last night the Sumner paper. I may get the journal wrong now. I think it was 2010. It might be Tobacco Control, but it might not be. But Sumner had done some

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estimates of what a clean nicotine inhaler, what its uptake would do to helping meet the President's Healthy Standards 2010, and found that in many scenarios, that alone would meet those goals.

MR. MYERS: But it only meets those goals if people actually switch to your product as opposed to use your product at some times, smoke cigarettes at other times, et cetera. So how do you --

DR. HUFFORD: First of all, even in that scenario, I would argue that there is some public health good taking place, not as much as you would like. But secondarily, as I mentioned, in the Light Touch regulation, post-marketing surveillance of how the product is used, I think should be a burden placed on manufacturers. I think these things would be of tremendous interest to the academic community as well.

So I think that's a great role for post-marketing surveillance to fully characterize precisely how the product is used. And I'd also argue that at the end of the day, that's really the only way to do it, is to get in the marketplace and

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let those market forces play out and see how the product's actually used.

MR. MYERS: So one last question, because you didn't actually say this. Your product currently isn't regulated by FDA. Do you support them being regulated by Light Touch?

DR. HUFFORD: I support them being regulated by Light Touch because I think that is in the best interests of public health.

MS. DILLEY: Any other question for Michael before we have -- if there is, I'd also like other panel members to come up. So Scott, Lars-Erik and Mike, come on up. Justine.

(No response.)

Q&A Session – Abby Dilley

MS. DILLEY: Okay. So as they're getting situated, we had one via e-mail for Lars-Erik. So when you're seated.

So this is from Joanna Cohen, Lars-Erik. "Yesterday Professor Carpenter --" in the IOM, his presentation on the IOM report -- "presented a letter from you to the IOM that indicated that

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Swedish Match would not be involved in any research among adolescents. What type of governance structure do you think would be appropriate for this type of research that is required by the FDA for MRTP applications?"

DR. RUTQVIST: Well, ideally, I would like that type of research to be conducted by independent university-based research groups. And in such case, the whole issue of governance wouldn't come up. And I think also that that would ensure a very high level of credibility.

If such research is not done by that type of group, I think in many of the models that, we've discussed, could be possible, including the models mentioned in the IOM report. And certainly, perhaps some of the models that are discussed in Jim Solyst's research article in the FDLI journal.

So there are many options, but, ideally, a totally independent research group.

MS. DILLEY: Anyone else want to speak to that particular issue, governance structure for particularly vulnerable or adolescent populations?

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(No response.)

MS. DILLEY: Okay. Any questions from the audience? Otherwise, we have other e-mails. Introduce yourself, please.

MR. DELMAN: Farrell Delman, TMA.

Great job, Michael. I thought that was a super address. And you were up at the SRNT, and we chatted a little bit about the MHRA and Light Touch regulation proposal that we heard from Mike Jarvis, I think it was who pitched it.

I'm still trying to get my hands around how CTP's going to address the population risk issues associated with the MRTP products. And certainly in the context of Light Touch regulation, that seems to create an interesting puzzle because population risk, as we well know in the public health standard, has yet really to be defined in terms of how you get your hands around it, in terms of how you design a model to capture it.

Since you're the innovation guru on this panel, I thought maybe you could kick it off, and others on the panel could comment on how if you

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were the director of CTP, what would you be doing to get your hands around the population risk issue and all of its potential forms -- in fact, we heard Neal Benowitz raise yet another one at the SNRT of, gee, look at all those e-cigarette smokers blowing vapor. Might that not increase something among non-consumers?

I mean, there are so many potential ways of framing the population risk issue. How would you as an innovator frame it? And then if anybody else cares to comment.

MS. DILLEY: Third-party governance on that.

MR. DELMAN: Yes.

DR. HUFFORD: So I shudder to think of myself in Mitch Zeller's position. I don't envy the job he has in front of him. From a population risk perspective, there's certainly, I think, some outstanding academic minds that can apply their knowledge and resources to research on that question. What concerns me -- and it's why I showed the Voltaire quote, that the perfect is the enemy of the good -- if we wait until all of the

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issues are perfectly articulated, that I fear is a recipe, whether through third-party governance or not, for the field to move forward.

These are extraordinarily important issues. I think the extent to which you're pursing a product, where nicotine's profile on health and health risks is so well established, that public health good is likely facilitated most by enabling those products to move forward, with combustible products, I think, probably having a very different threshold for evidence to be approved as a modified-risk tobacco product. And I think there's both science and history to kind of justify that particular position.

MS. DILLEY: Okay. I am going with another e-mail question.

"Many of the speakers talked about not needing a third-party governance model because they're already working with third parties, including CROs. But typical contractual agreements do not provide complete independence in the way that was discussed on day 1. For example, the

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funder typically has final say on research, agenda setting, study design, conduct analysis, and the ability to publish.

"Can the speakers comment on this model relative to the criteria discussed by Joanna Cohen on day 1, which included freedom to publish findings, even if negative, and protections against conflict of interest?"

DR. WALKER: Let me start by saying we talked about third-party governance. I mentioned the FDA at least in my talk. I really believe that the agency has the governance structure and the governance elements. But we didn't talk much about the TPSAC, which also has an important role to play in third-party governance. It's an independent third party. It helps the FDA with modified-risk applications. It could be used to address some of the scientific standards and some of the methodologies that we need to address.

There's no reason we can't have TPSAC meetings over the next 6 to 12 months on some of these critical topics to bring together thought

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from industry, academia, public health, the whole element of people to sit down and say, okay, how would you develop criteria around initiation? How do you address the issues of cessation, special populations?

So I think we think there's an increased need for ongoing dialogue, but there are mechanisms. There are things in place that have not necessarily been used to their fullest to articulate how we proceed forward.

I would agree with some of the comments earlier that we need to move forward. There's an amazing amount of innovation that's been occurring in the tobacco space over the last three to five years, and the innovation needs to continue. But I would also caution that when we do innovation, we make sure that the pre-market assessment is sufficient in terms of scope of science. We make sure we understand risks upfront, to the degree we can, and then we monitor those risks going forward for these new products.

So I think there's a balance between rush to

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market and good science. I think there's a need for pre-market evaluation of these products in the right kind of context, and then post-market surveillance.

MS. DILLEY: Anybody else want to respond to that question?

I guess I would have a follow-up question just in terms of, Michael, using your quote about "As in manufacture, so in science, retooling is an extravagance to be reserved for the occasion that demands it." I hear this tension from different comments on innovation, of public health standard, and transparency of data, and independence of research, conflict of interest.

Can you address that constellation of issues and whether a role for third-party governance does play a role, or it does demand something different, radically different?

Michael or anyone. I just used your quote, Michael. I liked the quote.

DR. WALKER: Can you maybe get a more specific question?

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MS. DILLEY: Yes. So I think Michael's quote was in reference to using a different regulatory process, so expediting review or some other things. The specifics on this workshop is around third-party governance, so in terms of looking at Joanna's criteria that she laid out and some other kinds of things, does it take a different approach to access to data -- I mean, I hear confidential business information is imperative because that drives innovation, but then there's also the public health standard. And this is a very different area for product development and review and approval.

So does that, too, require very different approaches, and can third-party governance play that role, and how?

DR. RUTQVIST: I think one should apply different standards, depending on what type of research it is. In areas where methodologies are very defined, very clear, let's say in the clinical trials, can you use a paid contractor to do that research, a contractor who is by definition not

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independent? Yes, I think you can because in those instances, it's very clear what should be done. The standards are very defined, and so there could be no discussion of how the work should be done.

I think it's more important to use independent bodies in areas without such clear standards also for setting research priorities because there could be bias in which areas you focus on, which areas you don't look at. And so from a broader perspective, I think there you need more independence.

MS. DILLEY: Any other comments?

DR. GRAFF: So I just wanted to follow up a little bit with that. With regard to contracting of clinical studies, there is a great deal of independence built into the Code of Federal Regulations currently with regard to principal investigators that are involved in those studies. For example, at any time, a principal investigator can stop the study if he feels that it's necessary.

So I've heard this bit about the independence of depending upon where the money is

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coming from, and I think we really have to think in terms of what independence is already built into the system as well. It's not a completely non-independent system just because I'm taking money from a pharmaceutical company or a tobacco company, depending upon where the money is coming from.

MS. DILLEY: Other comments?

DR. WALKER: Yes, let me just clarify a couple perspectives. I think we talked about in our discussion contract research being done in a sort of independent manner. I agree with the comments that Don made about nothing is completely independent and free from bias, which is why you need vigilance. But I would point out to you that we have, within the agency and within the TPSAC, and within the other processes of the agency uses, a tremendous amount of surveillance and vigilance about the industry research.

I would point out three things that I think about. One is people, one is process, and the other is power. So when I think about what the

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agency can do in the area of this research to help put standards in place, to help monitor research, study conduct, it occurs to me that they have people that have highly specialized skillsets. From the center director all the way down to office of science, communication, policy, you've got people who've worked in the field of tobacco control, tobacco research, for decades. You have people who understand the problems and the history. You have people who have science degrees. You've got a lot of the elements that need to be in place so that you can monitor and conduct research in a very transparent and a very ethical way.

In terms of processes, the model we're talking about, the contract research model, although not perfect in all circumstances is a very good model for which I think we can form the basis for much of the research we do going forward.

There is a fair degree of independence of the contract research organization from the sponsor. They do site selection, study monitoring. They do all the things that you would normally

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associate with independence and freedom. They select investigators. And I can tell you, having worked in industry for almost 20 years, when you work under FDA regulation and when you sponsor studies, you're always mindful of everything you do and how it might run counter to the FDA's perspective on your study. You don't want bias in your study because you know at the end of the day, you go before a review committee and before the agency, and you've got problems.

So I think there's people, there's a process, and, finally, we should not forget that the FDA has the regulatory authority. It has the power to set standards, to make decisions. And we may agree or disagree at the end of the day, but the agency is the regulatory body.

So when I think about all the elements that FDA has, I think we should really consider there's tools we can use today, we should use. We can perfect them over time if they prove insufficient. We can modify them. But we have constructs for third-party governance and effective clinical study

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conduct in place today.

MS. DILLEY: So questions, Corinne.

DR. HUSTEN: Corinne Husten, FDA. I just wanted to ask the panel, yesterday, one of the models that was put forward by Dr. Cohen was this idea that the independent organization was really more of an organization to put out for open sort of competitive proposals to do research to answer the specific question. And I guess I'd like to hear what the panelists see as sort of the disadvantages of that type of approach, where instead of directly contracting, it's a more open process where there's an independent review of proposals to assess the study strengths.

So anyway, I'd just be interested in hearing specific -- because that was a specific sort of model that was put forward, and I haven't really heard anyone talk about that model.

MS. DILLEY: Any response? I think everyone was here for that presentation. Michael?

DR. HUFFORD: I would just note, wearing my hat from my days helping to work in and grow a

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number of contract research organizations and sitting on innumerable project teams, both on the sponsor and on the vendor side, I think it holds tremendous intellectual appeal.

It concerns me a little bit of sort of, one, the mechanics of how it would work and whether it would potentially slow research considerably, is a real concern of mine. Do the projects get awarded to the lowest bidder among all competitive proposals?

If a company has other pharmaceutical and biotech clients, have medical directors that are on the phone with them every single day helping make decisions about how research is executed, if these products are sort of given to a third-party organization and kind of, then, the research is farmed out -- I just worry about the logistics of a little bit of how exactly is that going to work at the project team level? How is it going to compete with other pharmaceutical industry projects?

Especially around some of the sources of expertise. You know, again, it's just been my

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experience, kind of both being a medical director or working with them closely on the collaborative side, their role is so central in the drug development model, in the CRO model, I haven't quite gotten my head around how that would work with applied to these products when the source of expertise resides at the funding company, and how some of those decisions would be made or who even is going to make them.

I think a lot of CROs would not have the expertise would not have the expertise to make those decisions when it comes to modified-risk tobacco products because they just don't have the relevant technical expertise.

DR. HUSTEN: Just to clarify, I wasn't saying that the organization would be making any decisions. It's just purely a way to have an independent review of the research design and proposal, and to have -- maybe break the link a little bit between the funding and the actual research in the sense that the funding doesn't depend on -- it's purely on the expertise in the

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study design that they submitted.

So, for example, if you had a modified-risk tobacco product application and you needed three or four different types of studies, and one was around consumer perception, that particular interest would be put up for a competitive proposal for people to come in who have expertise in consumer perception to propose how they would look at that issue and design a study to give results.

Again, it's just potentially a way to address what we were hearing, was skepticism about the credibility of the research. I was just concerned about what you saw as the major flaws of that type of a potential design.

MS. DILLEY: Lars-Erik, I thought you spoke to that. I thought you spoke to that a little bit in terms of contracting out some of the --

DR. HUSTEN: I just want to clarify, it wasn't a decision-making body. It was purely to fund the -- peer review or to have an expert panel review the research proposals.

DR. RUTQVIST: I didn't particularly address

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the issue of consumer perception research, so my comment was of a more general nature.

MS. DILLEY: I just thought the mechanism of putting out design elements were -- it was part of some of your work.

DR. RUTQVIST: Well, it's what we did in the clinical trials, but I think what Corinne is referring to is something different

MS. DILLEY: Mike?

DR. OGDEN: I think that model might have some merit if you -- in some areas of MRTP research, as I carved them out in my presentation, you talk about basic tool development versus the sponsor's obligation to develop science specific to a product application, and then post-market surveillance.

I think to your question, Corinne, in the first instance of developing basic tools to answer fundamental questions, that seems entirely appropriate to me. And I think that's the way you framed your follow-up question. If you want to answer the question about consumer perception, you

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would seek competitive proposals or protocols on how to do that.

I think if you're in the second area, where it's product specific, I then would share Michael's concern. I think in my view, it falls to the sponsor to decide, in consultation with the agency, as to what an appropriate protocol would be. And if you went then at that point to go to some third-party structure and started shopping around different protocols, that could take quite a bit of time, again, without any a priori knowledge of which protocols might deliver more robust results, et cetera.

So I think it could be useful in some areas, but I think in the area of sponsor-specific work, I don't think that would work. But in basic tool development, perhaps even in post-market surveillance, there might be some merit to that.

MS. DILLEY: Matt, and then we had some other e-mail questions.

MR. MYERS: This is to Don. In trying to figure out the role of organizations like yours

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versus some sort of independent third party, I was trying to get a sense of when a company comes to you, the relative role of your organization versus their organization; and, A, developing the study design; and, B, even more broadly, deciding what it is that needs to be studied.

DR. GRAFF: Sure. So it really depends on the company that comes to us. So we have some sponsors, both in the pharmaceutical industry and the tobacco industry, that come to us with fairly complete study protocols and designs, and they have a really good understanding based on what they might have done in the past so that they have a really good idea of the best design that they have in mind for this particular study to answer the questions that they want to have.

On the other end of the spectrum, we sometimes have -- again both in pharmaceutical and tobacco sponsors -- people who come to us with really no idea. They have a basic idea of what it is that they want to try to find out. They may not have a specific objective yet at that point, but

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they want to evaluate a product. So how do we best go about that? And there's really everything in between that we might see as well.

After we talked at the break, one of the things that I thought about was, currently, we probably write and help design I'm going to guess, 50 percent or more of the ideas that come to us from the tobacco industry. On the pharmaceutical side, we really have input on writing the protocols on about 20 percent.

Now, that's not to say we don't have some input because every study that comes to us, if we're going to conduct the study, we have an operational review so that the clinic knows -- can handle the logistics. And if we do the backend data analysis and data interpretation, we have our clinical pharmacologist and statisticians review as well. So we do have input in those areas.

Now, in some cases our input is taken and politely set aside. In other cases, it's been incorporated into the designs of the studies. And, again, this is for both the pharmaceutical and

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tobacco industry.

MR. MYERS: So as your organization does its work then, do you take a look at -- if somebody comes to you with a study design and say to them, well, that's not really going to tell us whether or not the product is safe, or in the case of tobacco where it's a complex product, if the change you made, we can measure whether or not you've effectively made the change. But it's not going to tell us whether or not the product causes less disease.

DR. GRAFF: Right. And so I think where we're at right now, at least with Celerion, we're not to the point yet that we're evaluating disease. I think we're really good at the exposure part of that. And so that's probably one of the gaps in the company that I work for right now is, okay, we had a really good idea of the exposure of these products. We can evaluate them differently, dual use, single use, cessation, the whole -- we've got a plan for all of that.

It's now taking it to the next step, and

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that is, evaluating these things long term and how are we going to evaluate the health risks of those. Those types of studies are ongoing, but they're really sort of in their infancy, in my opinion.

MS. DILLEY: Thank you.

Justine, you wanted to comment?

MR. APELBERG: Abby, can I just make a quick comment there? What kind of -- sort of chemical smell –

(Discussion off the record.)

MS. DILLEY: Justine, sorry. Go ahead.

DR. WILLIAMSON: I'm relatively new to my role of -- I'm head of biosciences, so I'll sort of speak to as much detail as I know. But we have -- and we're about to publish on a reduced toxicant combustible product clinical study. We'll be publishing the results of this next week. And when it came to designing the protocol, we're going a little bit back in time, yet we were very much consulting with literally as many people as we could, because this is an area that was new to us, so we were talking to external experts. We were

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speaking and listening to the CROs to get their expertise.

So I think it's a learning process. We took the learnings from that. We've got the second clinical study data now in lockdown, and I think it's about -- we put our protocols out there. We're putting our data out there. We may make mistakes, but I think it's just about keeping -- putting the data out there, and let all of us keep looking at it and seeing what are the right protocols for us all to be using.

MS. DILLEY: Okay. I have an e-mail question. This is from Mark Parascandola, and it's to you, Mike.

"So presumably, RJR is already conducting some research on tobacco products. Would you consider making information about all ongoing research projects publicly available? For example, this could be done in a format similar to clinicaltrials.gov, providing summary information about study aims, methods and results."

DR. OGDEN: I think the question

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was -- well, based on current research, my understanding is all of our clinical trial research is registered at clinicaltrials.gov. That was not true going back 8 or 10 years, but the information is publicly available of the types of studies we've done. Certainly, information on those studies is available to FDA as being produced through the health documents discovery, et cetera.

So I think with our view to conforming with societal expectations, I think, yes, we would entertain that notion of -- to the extent we're not doing it now, we would entertain the notion of making the visibility of those trials to the appropriate level. Our intention is to publish and present those results in due course. As many have mentioned, there's some barriers to doing that in an expeditious way with industry funding, but certainly, all of those data then become transparent, fully transparent to FDA.

MS. DILLEY: Questions from the audience, or else I'll go back to the e-mails?

MR. MOYNIHAN: Michael Moynihan, Goodrich

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Tobacco. I think I've been able to clarify the question I failed to articulate yesterday, but I think some of the speakers today have actually answered it. But nonetheless, the question I wanted to ask was, would FDA approval of one or more third-party governance entities increase the production, or the dissemination, or the credibility of research to support modified-risk tobacco product applications?

MS. DILLEY: So you'd like to hear the panel member --

MR. MOYNIHAN: I'd like to hear each person answer that in a simple, not yes or no, but as close as possible.

MS. DILLEY: Anybody want to start? Scott?

DR. OGDEN: What was the question?

MR. MOYNIHAN: The question is, I'm concerned about sort of a fairly specific answer in response to Recommendation 10, really, which I think some of you have answered. But so the question is, would FDA approval of one or more third-party governance entities increase

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production, dissemination, or credibility of research aimed at supporting an application for a modified-risk tobacco product?

MS. DILLEY: So specifically an application. So I think some people addressed those in their comments, but he'd like you to respond to that. It could be, it depends, yes, no.

DR. WALKER: Maybe, maybe not. I think it depends on the framework that you're talking about. It depends on the questions you're asking. I think it depends on whether the research is of a general nature or if it's product specific.

MR. MOYNIHAN: Only product specific.

MS. DILLEY: Only product specific for MRTPs in particular.

DR. WALKER: So our perspective is that that process needs to be gone through the FDA. We think that the FDA has and can acquire the requisite knowledge and expertise to make those kinds of determinations in a pre-market setting.

Do I think a third party on top of the FDA would be more efficient? The answer is probably

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not. I think it would be less efficient. It really depends, though, on how it's structured, the questions that are being asked.

So I guess that's my maybe, maybe not. You'd have to be very specific about the kind of structure, the kinds of considerations, and the level of authority that you give to such a governance body before I could really answer the question.

MS. DILLEY: Justine?

DR. WILLIAMSON: I think, in general, if we have a defined structure, if we have defined tools, it will make everyone's life easier because we will know then where we're trying to get to. And I think probably because there is uncertainly, especially around some of these tools, around abuse liability and where we go with those, that is at the moment probably slowing things down -- once that's in place and is agreed by everyone, then I think potentially, yes, things could increase in speed.

MS. DILLEY: Lars-Erik?

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DR. RUTQVIST: The definition of an MRTP is very complex and requires many different types of studies. Would it increase credibility if these studies have oversight from third parties or involve third parties? Yes, I think it would.

Would a sort of overall third party that oversees the whole process add anything to this? I'm not so sure.

DR. OGDEN: I think I would echo many of the comments I've heard, just to summarize some of those. I mean, I share -- we share Jeff's concern about the notion of the word "governance" and what that means, and does that -- it appears to imply relinquishing of either the rights or the responsibility of either the sponsoring industry, company, or the agency. That's problematic.

If governance were to be imagined as TPSAC review, which is specifically authorized in the act, no, not a problem. As it goes beyond that, I think you have to be -- we would approach that with caution. And at this point where we sit at the table is that that's not what's required. There's

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no model for that, and it would be difficult to see how it would add value.

Now, that's not to say that's true in all cases, but, specifically, I think your question, Michael, about specific product pre-market research, our position is that that would slow things down and would not be in the best interests of the process or moving the modified-risk tobacco product to market in a timely way.

MS. DILLEY: Michael Hufford.

DR. HUFFORD: So my one word answer would be maybe, and, Michael, to reiterate something that I said at SRNT last week, I think investors live on a teeter-totter between fear and greed. And regulatory uncertainty is an enormous part of the fear equation here that freezes capital, which is frozen energy, I think, from coming into the space and funding more innovations to come forward.

I think it's -- the agency may be completely aware of this. I just don't know, that lack of clear action is interpreted by many folks as a concern, as a barrier, as a reason not to move

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forward. So I would see any clear action that clearly articulates what the path forward is, I think, will do a service to bringing innovation and capital into the space.

MS. DILLEY: Donald?

DR. GRAFF: So I'm going to use two words, and I would say not necessarily. So my viewpoint is again from a very operational level, is having the framework in place or at least some idea of what it's going to take to get a product approved, with some specifics behind that. And so start there, and then start working your way back and determine whether or not a third-party governance structure is actually required. So instead of okay, let's define this structure and then figure out how it's going to work, start from the end and sort of work your way back.

MS. DILLEY: Scott?

MR. BALLIN: Something I said this morning about the bureaucracies, we don't want to create exorbitant bureaucracies that actually have negative effects on trying to accomplish a public

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health goal. That happens all the time.
So I would say it depends on how it's done, but we don't want to sacrifice progress by creating bureaucracies, but we also want to make sure that the system works properly and there is proper oversight. Now, whether that's done by FDA and it needs to talk to people or saying we need some additional advice on this, I don't know how that could be done, but it's an alternative instead of setting up something that's too complex.
MS. DILLEY: I have an e-mail question.
"This is a follow-up to Dr. Cohen's e-mail question. Both Mike Ogden and Justine Williamson mentioned that potential need for third-party governance regarding vulnerable populations. I think this is in the research tools category, e.g. adolescents. What are your thoughts regarding the most appropriate governance structure to conduct this type of research?"
Justine, do you want to start on that?
DR. OGDEN: Well, I touched on some of this in my prepared comments earlier. I mean, I see

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that as an area that has potential concerns. I mean, we're aware of what those concerns are. I think if that type of research is required for a modified-risk tobacco product application, and it appears that it is, then our view at this point would not waiver, that that is the responsibility of the sponsoring company to conduct that research.
We have made it clear with FDA, going back two years now at least, by letters, by sending draft protocols, and by asking for clarification as to specifically on this point. Our position is that we have tools that are appropriate and we believe applicable in that space. But we will not conduct those types of research unless or until FDA is explicitly clear with us that that information is required and that they -- at least we have a meeting and we agree to the protocol.
So under those circumstances, I would say at this point, we have not done that research yet, but I think that it's possible that we would. If that becomes a necessary component and we cannot get that direction from FDA, then I think we're at a

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standstill unless we find some third solution. And under those scenarios, if we cannot make it work directly with the agency, then we would explore other options, and a governance model might be appropriate there.
MS. DILLEY: Justine?
DR. WILLIAMSON: Similar lines.
MS. DILLEY: I think this is a follow-on question that's very similar, that you indicated "that BAT has expertise in risk perception and post-marketing surveillance. Thus, do you feel that BAT could sponsor and conduct this type of research in support of MRTP applications? And if third-party governance is needed for this type of research, what type of governance model would you recommend?"
DR. WILLIAMSON: So maybe slide was a little misleading. I can't remember what was in the banner, but these were areas that we are developing in. So right now, no, we do not have enough expertise in these areas. So that's why we are looking to dialogue on these areas and speaking to

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the correct experts in the field to develop the expertise in house.
MS. DILLEY: And there was another question to you, Justine, on the same e-mail.
"On your presentation, you indicated that in the future, you would consider partnerships with NIH. Could you please elaborate on this?"
DR. WILLIAMSON: I think --
MS. DILLEY: What would an ideal partnership look like, part of that.
DR. WILLIAMSON: So, yes. I mean, our understanding is that the TCORS and the NIH-type funding don't exclude the industry. But what we would sort of -- what we were saying in that statement there is that for those research partners who are looking to take on that funding, and they need some additional support, that we may be able to give them.
So like any expertise we have, maybe our analytical services -- one example that institutes have been coming to speak to us about is our experience around whole smoke exposure systems. We

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are doing a lot of work in that area, and a lot of parties are interested in working with us on that. But because of their restrictions via taking funding, they're unable to talk to us about that.

So what we would say is if those guys were going to want to do work in that area, then maybe they want to go down that route, and we could then potentially offer advice, support, help through those more transparent and organized funding mechanisms.

MS. DILLEY: Other questions from the audience?

(No response.)

MS. DILLEY: I've got another question from Mark Parascandola.

"The tobacco industry presenters mentioned or described ongoing research efforts around tobacco products and harm reduction. Some are publishing papers and making presentations on their science. To be fully transparent, the companies could make detailed information publicly available about all studies they conduct, including

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disclosing study aims and methods before work is started and making all results and data public.

Can each of the presenters describe their own company's plans for scientific data and information sharing?"

DR. WILLIAMSON: And I probably spoke to this one a little bit before. As I said, we're publishing next week on our reduced toxicant combustible clinical study that we ran a couple of years ago now. Now, that's the results that we were publishing. We're already published the methodology. We've already published on the technologies included in that product.

So that's very much the approach we're taking, is just to publish as much as we can along the road.

MS. DILLEY: Other comments, Jeff?

DR. WALKER: From our perspective, we are being very transparent, very forward with the agency with regard to our studies. When we want to think about proceeding forward in a new area with a new product, we meet with the agency and tell them

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our plans. As we would anticipate starting clinical trials, we would meet with the agency before starting the trials to make sure the protocol and the methodology is correct, meet with consultants, meet with contract research organizations.

So our efforts right now are focused within the regulatory framework, and we do not have at this point in time a mechanism to talk about, particularly, pre-market studies. There's certainly particular issues around competitively sensitive information where you wouldn't want to necessarily tell everyone what you were doing because your competitors would sort of be alerted to, well, gee, they're working on this new product. Maybe I should work on the product, too.

So there's some really practical limitations to early disclosure of research. I think we're going to work through those. I think we're still working through when it's appropriate to list on clinicaltrials.gov. And I think at the present time, as we get ready to conduct large clinical

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studies, we would want to make that information available, but in an appropriate timeframe, in the appropriate venue.

MS. DILLEY: Lars-Erik?

DR. RUTQVIST: When it comes to clinical trials, we obviously follow the pharma model and register the trials at approved clinical trial sites. Otherwise, when it comes to other types of research within academia, there is no sort of accepted way of disclosing that type of information. So we obviously disclose it to the FDA, but apart from that, we haven't really considered using any model of our own that is different from what you would normally do in academia.

MS. DILLEY: Yes. And I think this question is less specific to FDA because they don't disclose the information publicly, but it's the broader, the public disclosure.

DR. RUTQVIST: Yes.

MS. DILLEY: Michael?

DR. OGDEN: Very similar to the comments

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previously, I think there's appropriate ways to disclose research, and then there's perhaps inappropriate ways to disclose research. And in this vein, I'm talking about the competitive nature of things that Jeff spoke about. And that extends not just to the fact that you're working on a product, but how you're evaluating it.

We have SOPs in place for all preclinical chemistry and in vitro and in vivo toxicology testing. We have protocols that we use for clinical trials. To simply make that publicly available divests us of a significant amount of information that others would like to have.

We know there's been a mad scramble around the world for a couple of years developing laboratory capacity and methods for harmful and potentially harmful constituent testing. If we were to put all of our SOPs out there, then contract labs would pick that up, and there would be competition there that may not always be in everyone's best interest.

So I think that the timeliness, certainly

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the right way to present that information. We do publish. We do present. But there's a lag there because of just the fact that you're investigating a certain type of product. But if you look back over the course of the development of a premier cigarette, for example, culminated in a nearly 500-page book that laid out all of that information, again, it's not raw data, but then I'd fall back to where my previous colleagues were. In an FDA context, all of those raw data, then those are perfectly transparent and available to the FDA, including all SOPs or constructions, and everything else that governs the conduct of that research.

MS. DILLEY: I think the Medtronic example and the open-data access project looked at the timing. So your point about timing and pre-market, I think they're trying to figure out timing as well, but also make a commitment upfront to -- I think that's what's Mark's asking is kind of an upfront commitment of publishing that data at some point.

DR. OGDEN: Well, I think that's an

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interesting model, and I was interested in that because as I heard the presentation and, in fact, I asked a clarifying question, he described more than a dozen studies obviously over probably that many years at least, and then additional information comes to light.

So I think once you've done clinical work in a pre-market mode, a product hopefully in a future world gets clearance. It goes to market. Other studies, I mean, the sponsor continues to do research. Others pick up the product and do their own research, and now you build a larger body of data.

Particularly if findings start to point in different directions, I think at that point, it is an interesting model to consider, okay, let's bring all of this together and try to find out what the real answer. And maybe it's simply a difference in methodology or statistical methods or whatever, but I think in that instance, that is an interesting model.

MS. DILLEY: We'll finish out the rest of

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the panel. Michael, did you want to speak to that issue?

DR. HUFFORD: Just that my colleagues and I all come from a world of drug development, so we absolutely intend to proceed down that path, filing everything on clinicaltrials.gov, being completely transparent with the agency, publishing our findings, and certainly take the CTP's lead. If the expectation is to make even raw data publicly available, then we'd follow that lead.

MS. DILLEY: Don, you want to add anything?

DR. GRAFF: No.

(Laughter.)

MS. DILLEY: Scott? No. Okay.

So we have maybe time for one or two more questions. I'm out of the e-mail questions, so I don't know if there are any more coming. Okay.

MR. DELMAN: Farrell Delman, TMA. I'm still suffering something of a disconnect in this whole conversation, based on information that you see regularly. I saw it the first time, I think, when I was at the SRNT meeting four years ago, when

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Dorothy Hatsukami presented a relative risk continuum. And at one end, we had NRT. At the other end, we had cigarettes. Snus was closer to NRT. E-cigarettes were not on that first chart. They've only kind of joined the chart in more recent presentations.

When you look at these categories of tobacco products, there does seem to be a certain sense out there -- maybe it's just intuition, or maybe people have gotten ahold of some epi data from Sweden, or there's an assumption that if you inhale a tobacco product, the combusted tobacco product, it's different than if you don't inhale, like with a cigar. So it might have a different place on the spectrum. That's one observation.

Another observation -- and then I'm going to put them together -- is that we're shortly going to be dealing with tobacco products standards, right? And when you look at the TCA timeline, you see that tobacco products standards are likely to be a source of conversation. The docket will be open and so on. And it's certainly also the case, many

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of us are expecting, deeming regulations, for all tobacco products to be shortly presented at the April deadline or whatever, results in deeming regulations.

This is all by way of saying that it seems to me that in these conversations about industry-sponsored research, we're always talking about a brand that companies will be bringing to the table, and historically FDA has operated at the brand level. Companies sponsor something. They bring their data. FDA reviews it.

I'm wondering if the panelists could address the question of whether the governance issue could be divided, say, over product categories as one set of issues that FDA may wish to address as a product category, and the brand issue within a product category.

For example, it would seem to me that if I were engaged at CTP, I sure would like to have a relative risk continuum. I would like to have some idea, certainly based on the impacts on the consumers themselves, of what the individual

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product's risk levels are, safety issues, but I'd also like to know -- I'd like to see a relative risk continuum that somehow incorporated population risk issues into it as well.

That would be something that FDA should want to do itself, through contracting research and getting results from the best experts out there, and that individual companies then might end up having a set of standards and rules for the kind of research that would be appropriate for individual product categories for which they would wish to have a brand in, and present the data to FDA the way we've been talking about it, mostly during this session.

So I guess I'm wondering if separating product category from brand makes any sense at all, in light of the TCA timeline.

MS. DILLEY: Well, that's a different take, but I think Michael Hufford touched on that, somewhat, in terms of categories of relative -- I guess I would say you're talking about relative risk. But any other comments on that?

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DR. RUTQVIST: As you know, there's a lot of documentation on long-term effects of a number of combusted tobacco products, and there is a lot of information on long-term effects of some smokeless products. And I think the best documented product there, as you suggested, is Swedish snus.

Now, whether category-specific information at all is interesting to the FDA, I don't know. I'm not a lawyer. But it's my impression that the FDA is obligated to focus on product-specific information.

As a scientist in this area, if you have a nicotine or tobacco product that is smokeless, it is likely that the long-term health effect profile of that product is more similar to the ones in that product category that we know about, like snus, rather than smoke products. But that is just conjecture. I mean, you don't know that.

It's my impression that the FDA needs product-specific information. I don't know if they're interested in category-specific information.

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MS. DILLEY: Any other comments on that?
DR. OGDEN: I agree with Lars-Erik. I think at least our experience and expectation is that FDA is interested in product-specific information for, for example, in modified-risk claim.
But to answer your question, I think sort of categorical differences are probably best not handled through the modified-risk pathway, but through health warnings. And many, if not all, know that Reynolds has filed a citizen's petition with FDA, challenging one of the smokeless warnings, the one that was highlighted this morning, that says smokeless tobacco is not a safe alternative cigarette. That's a half truth at best.
So a more appropriate warning label there I think would go a long way to carving out that categorical difference that virtually everyone agrees has been firmly documented over a decade or more.
MS. DILLEY: Any other comments? And we're going to wrap up. Don?

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DR. GRAFF: Just one comment briefly on that. So it's my interpretation of the regulation that's out there that with one of these applications, you're going to have to do a substantial amount of comparisons to not only products within a category but across categories as well. So I think one of the things that's going to come out of these per product/per brand applications is a great deal of product information across -- on a much broader basis.
So I think indirectly one is going to result in the other one. Now, what the FDA decides to do with that, that's for them to decide. Maybe that goes into product standards. Again, really, that's up to them.
MS. DILLEY: Any other comments?
(No response.)
MS. DILLEY: I want to thank the panel members again for your time and presentations.
(Applause.)
MS. DILLEY: And I will turn it back over to David Ashley to wrap it back up.

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Concluding Comments
DR. ASHLEY: I would like to thank particularly all the invited speakers who came. I'd like to thank those folks who came and presented in the open public time. And for everybody else who's participated in the workshop, those of you who came in person, those of you who joined us remotely, and just give you my sincere appreciation for that.
Also, I'd like to thank everyone who participated in the questions and answers, and asked very good questions, very thoughtful questions, and I really appreciate that.
A couple of things I took out of today's discussion were, particularly, areas around the challenges of how to address the range of products that are made or derive from tobacco. Clearly, it presents some significant challenges to FDA and to the industry both on how to have a consistent process and -- I still want to go back to Scott -- how to be consistent and flexible at the same time.

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There are also a couple of things that came out that were clear differences among the speakers today. There were different views on to what degree product-specific research should be carried out outside the industry versus inside the industry. There were some differences of opinion on making MRTP-supporting data available to the public, whether that should be made available or not made available.
But there were also some common themes that came out, particularly on the need for specifics on how to conduct studies and what specific studies are needed. Clearly, that is a work in progress and will continue to be for a while.
Also, the major challenges around youth and other subpopulations, which was highlighted in the IOM report, unfortunately, no one stepped up and said here's how you solve that problem. It is definitely an issue. It will continue to be an issue for some time as we work through that, and there's clearly a common theme around that.
As I said at the beginning of day 1, the

purpose was to provide an opportunity, in a public forum, for FDA to hear from those with experience and informed opinion on the issue. We found the presentations and the subsequent discussions really to be very, very useful. I've taken a lot of notes. I know others have taken notes. It's been very useful to have this discussion. There is a great deal of challenges that are still out there.

As a reminder, we're planning to open a public docket for public comment. When that opens, we'll be posting the information on the CTP website, so you can also sign up for updates from CTP by visiting the website. So please make sure you put your comments in there. Particularly those of you who didn't get a chance to speak up and add to that, please add your comments there.

We see this workshop as an initial step. This is one step along this journey. It's a very complex topic, and we plan to move forward. And, again, please take advantage of the public docket to provide us with whatever information you have that will help guide us along that way.

Adjournment

DR. ASHLEY: So thank you all for coming. We appreciate your attention and appreciate the good questions and the discussion back and forth, and I hope you have good travels getting back.

(Whereupon, at 12:50 p.m., the meeting was adjourned.)

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